NCCN/JCCNB Seminar in Japan
April 15, 2012

Case study 1

Rie Horii, M.D., Ph.D.
Division of Pathology
Cancer Institute Hospital,
Japanese Foundation for Cancer Research

Present illness:

A 50 y.o. premenopausal woman was found abnormal mammogram results and referred to Cancer Institute Hospital.

Physical findings:

No mass palpable in either bilateral breasts nor bilateral axillary fosses. No nipple discharge.

Family history of breast and ovarian cancer: none

Past history of breast disease: none

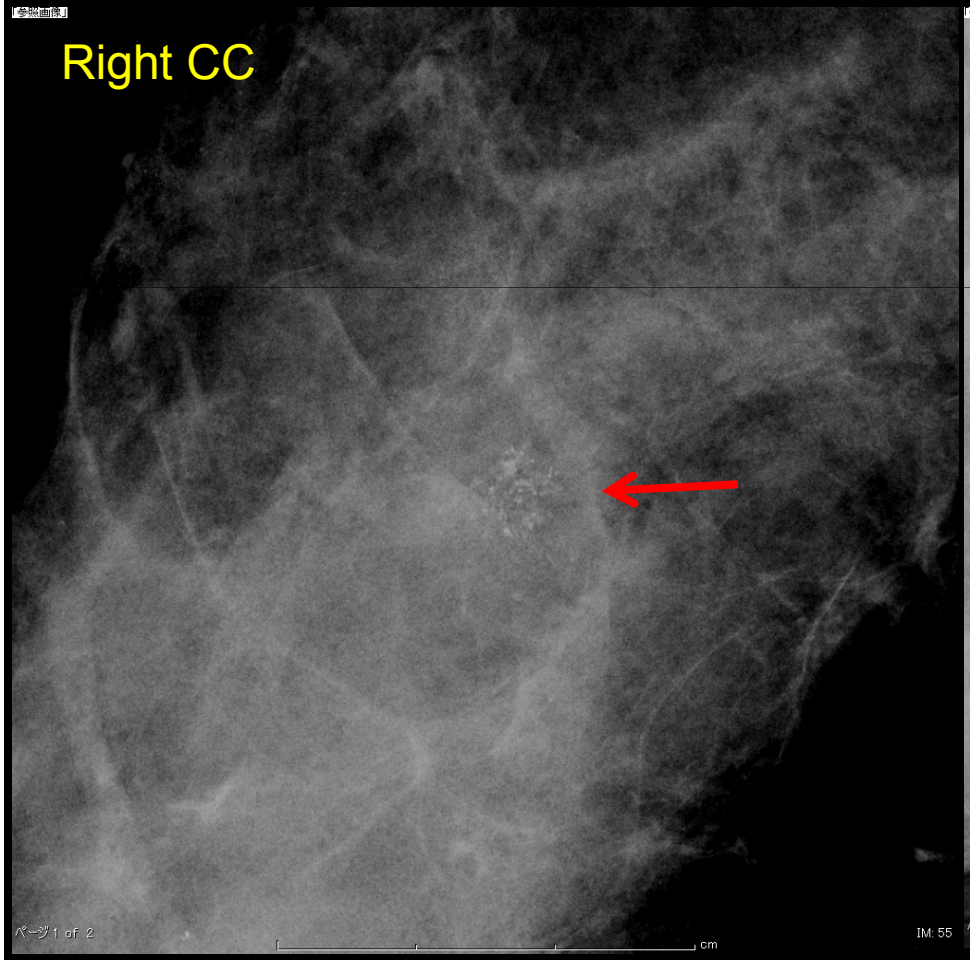
Gravitates: three times, Parturition : twice

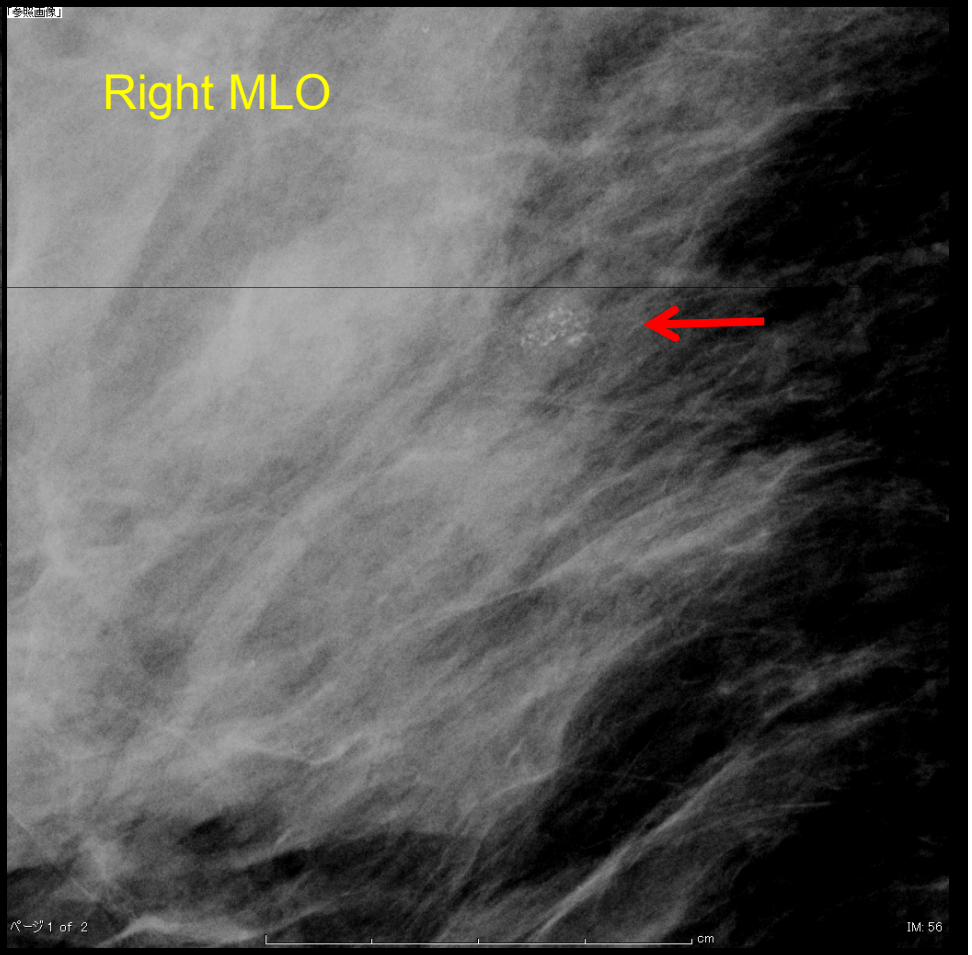
Mammogram at the initial visit

Right outer upper area

Amorphous grouped calcifications in scope of 5 x 4mm

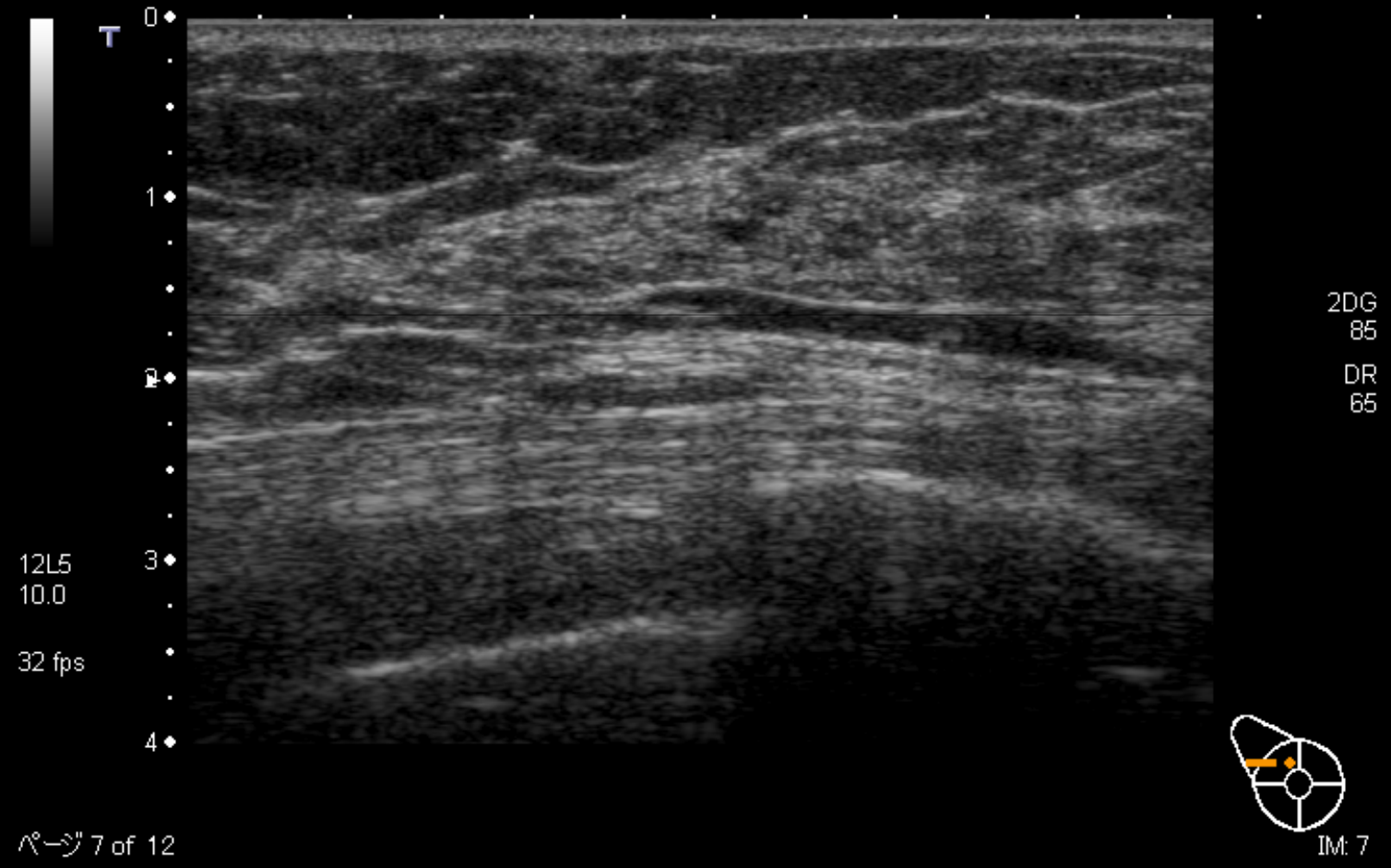
Category 3-2 according to the Japanese MMG Guideline





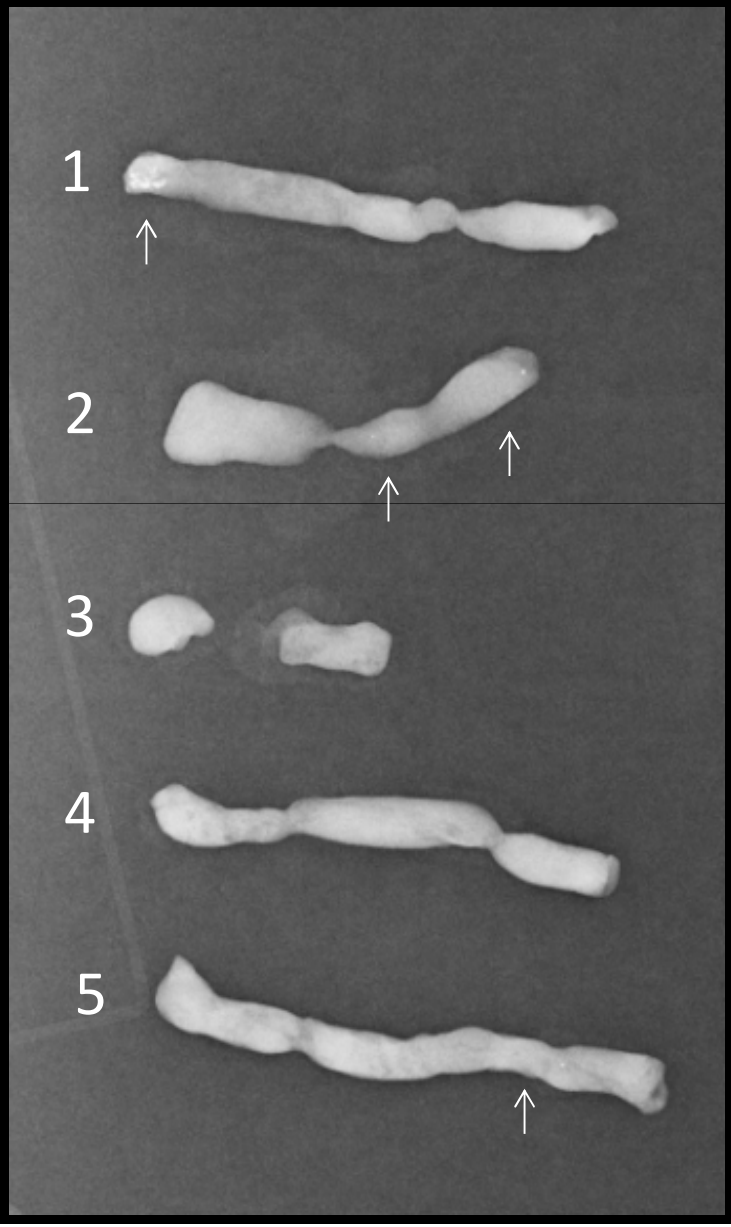
Ultrasound at the initial visit

Bilateral breast cysts (Mastopathy)



Stereo-guided vacuum assisted breast biopsy
（Mammotome™ biopsy）

- 5 samples of 11 gauge needle biopsy
- Micro-calcifications were confirmed at 3 of 5 samples.
- Micro-mark was inserted.



Pathological findings of biopsy specimens

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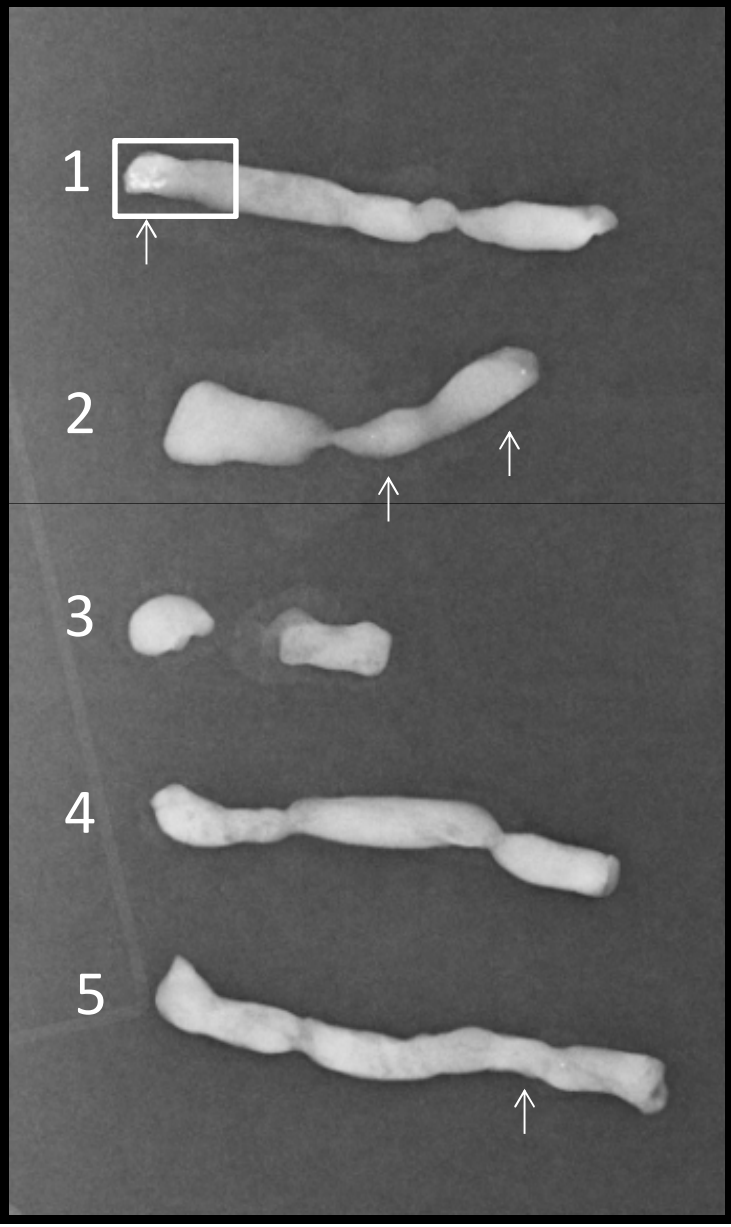
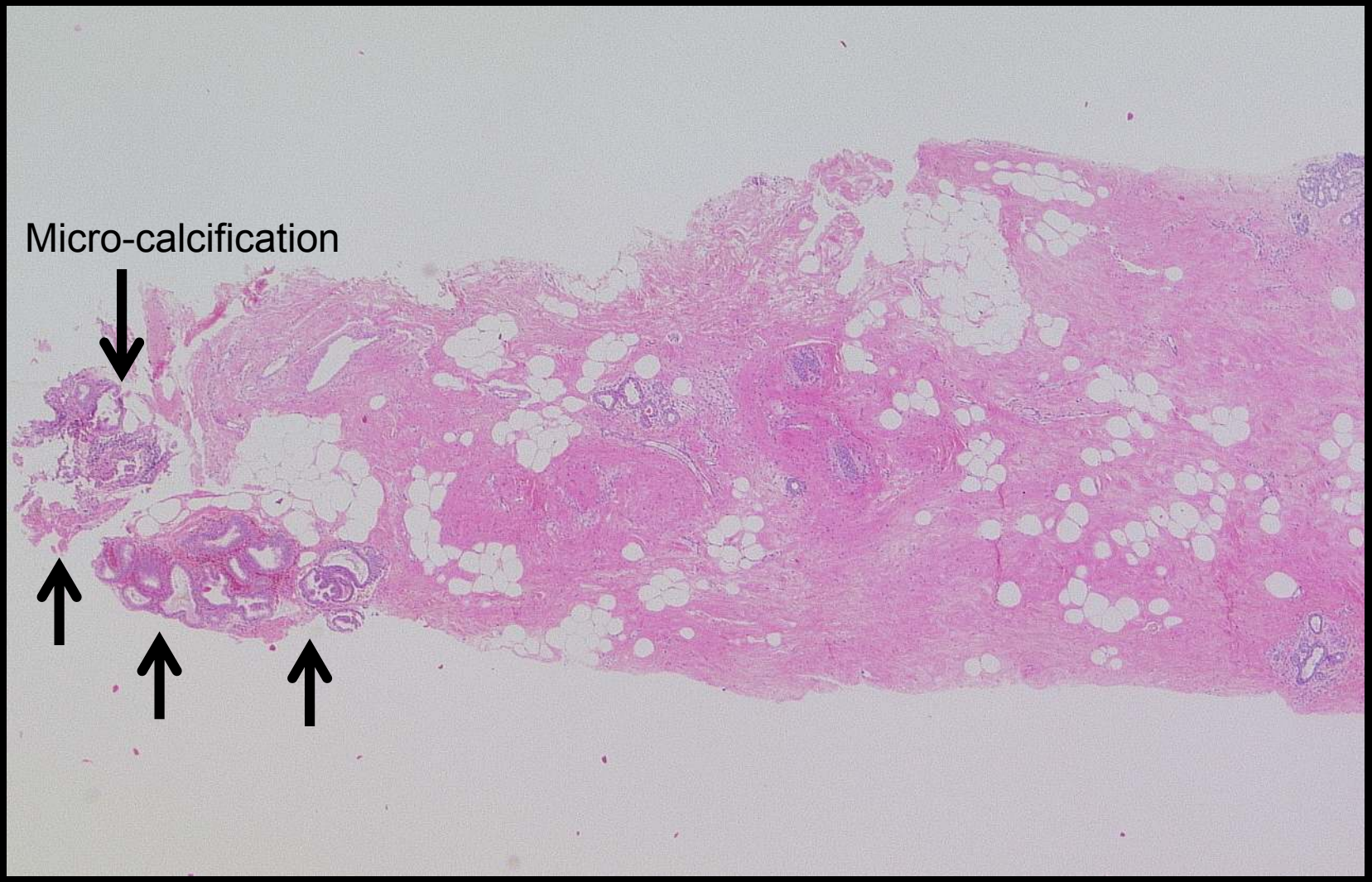
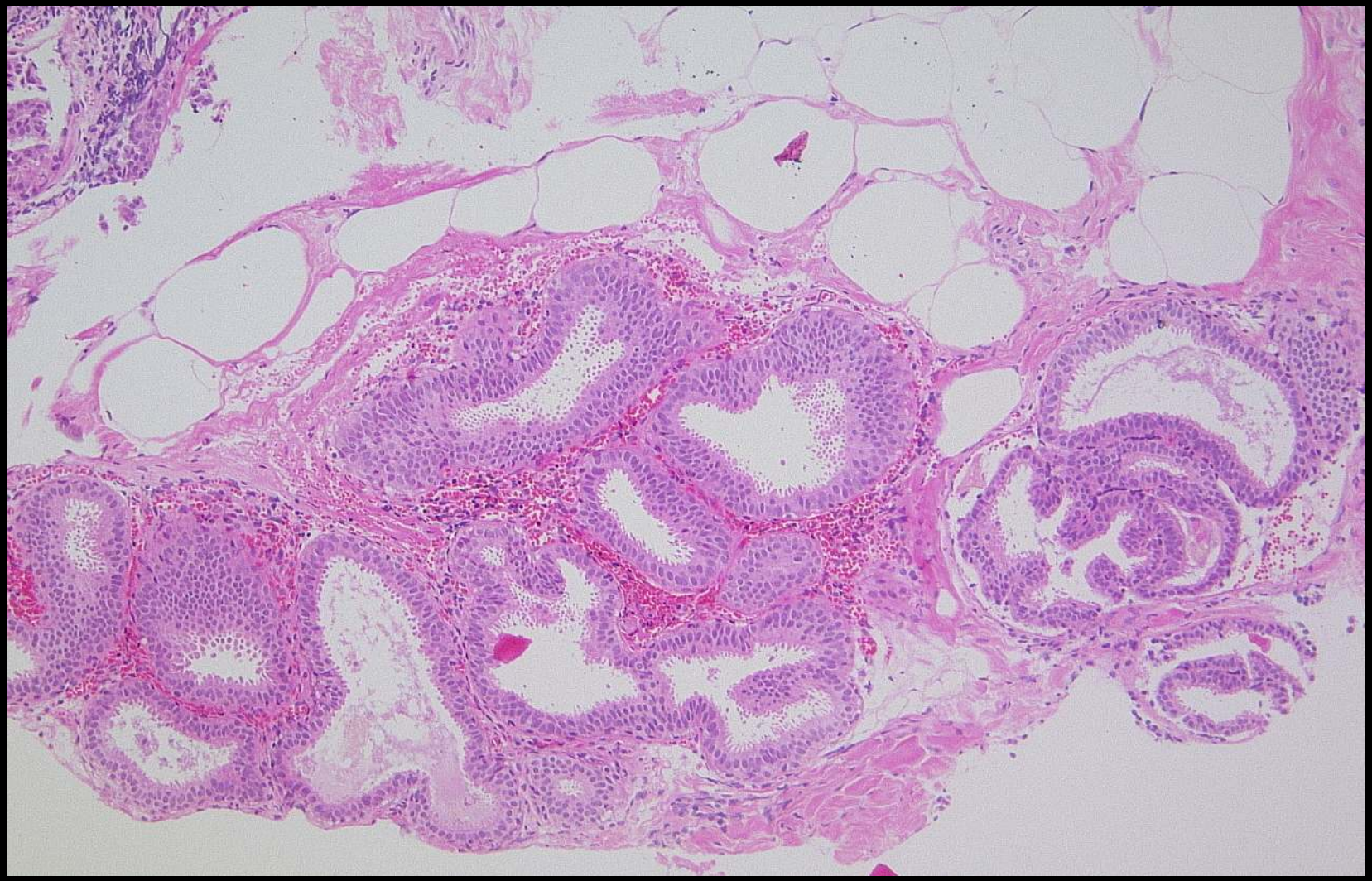




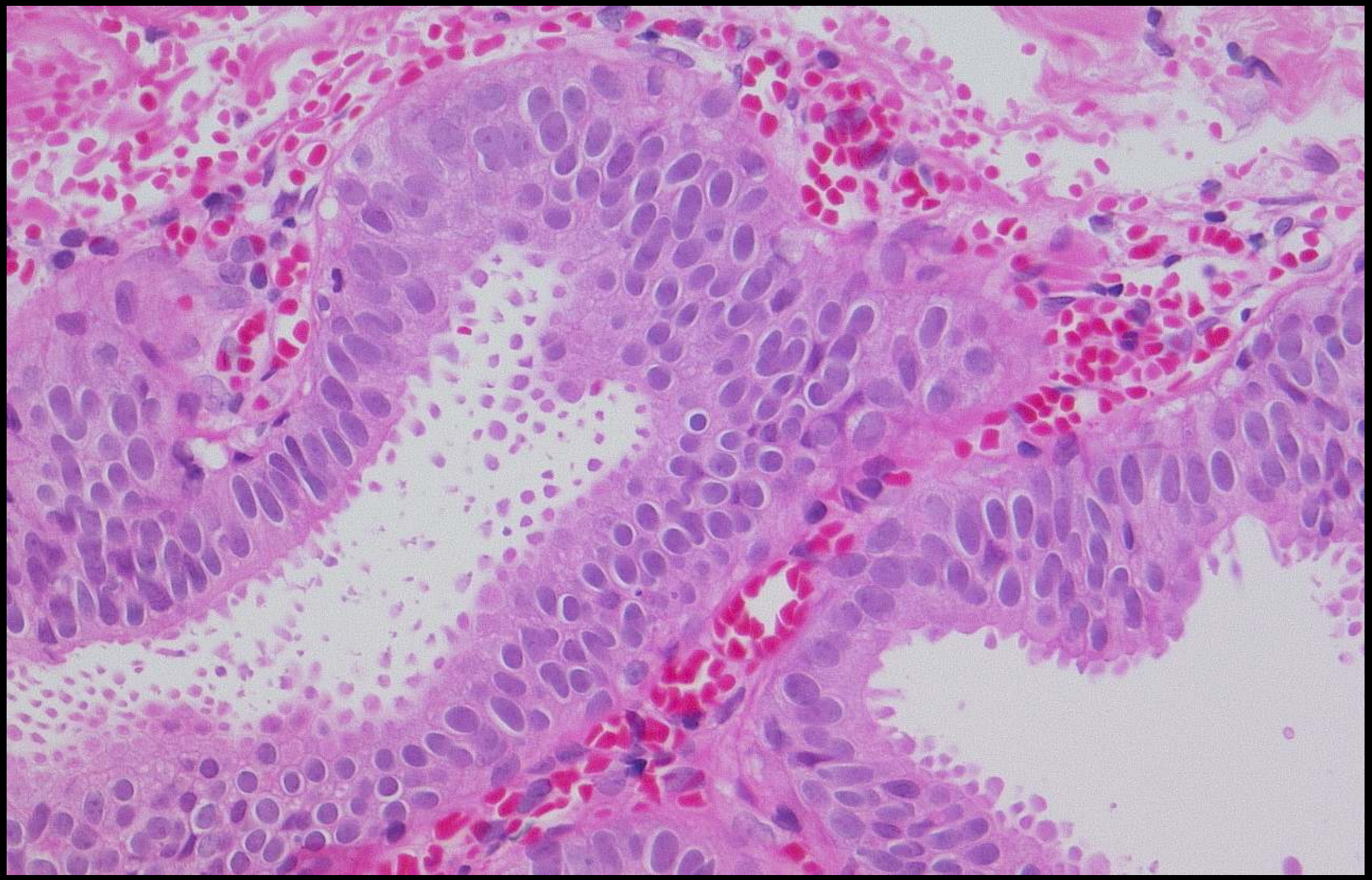
Original magnification: Objective lens X2

Atypical in situ lesion with micro-calcifications



Original magnification: Objective lens X10

A terminal duct-lobular unit with distended acini and secretory luminal contents. The spaces are lined by one to three layers of monotonous atypical cells.



Original magnification: Objective lens X40

These cells are columnar and have eosinophilic cytoplasm and oval nucleus with mild atypia. Cytoplasmic snouts are evident. The myoepithelium is indistinct. This lesion was comparable to flat epithelial atypia (FEA) according to the WHO histological classification.

Stereo-guided vacuum assisted breast biopsy
（Mammotome™ biopsy）

- 5 samples of 11 gauge needle biopsy
- Micro-calcifications were confirmed at 3 of 5 samples.
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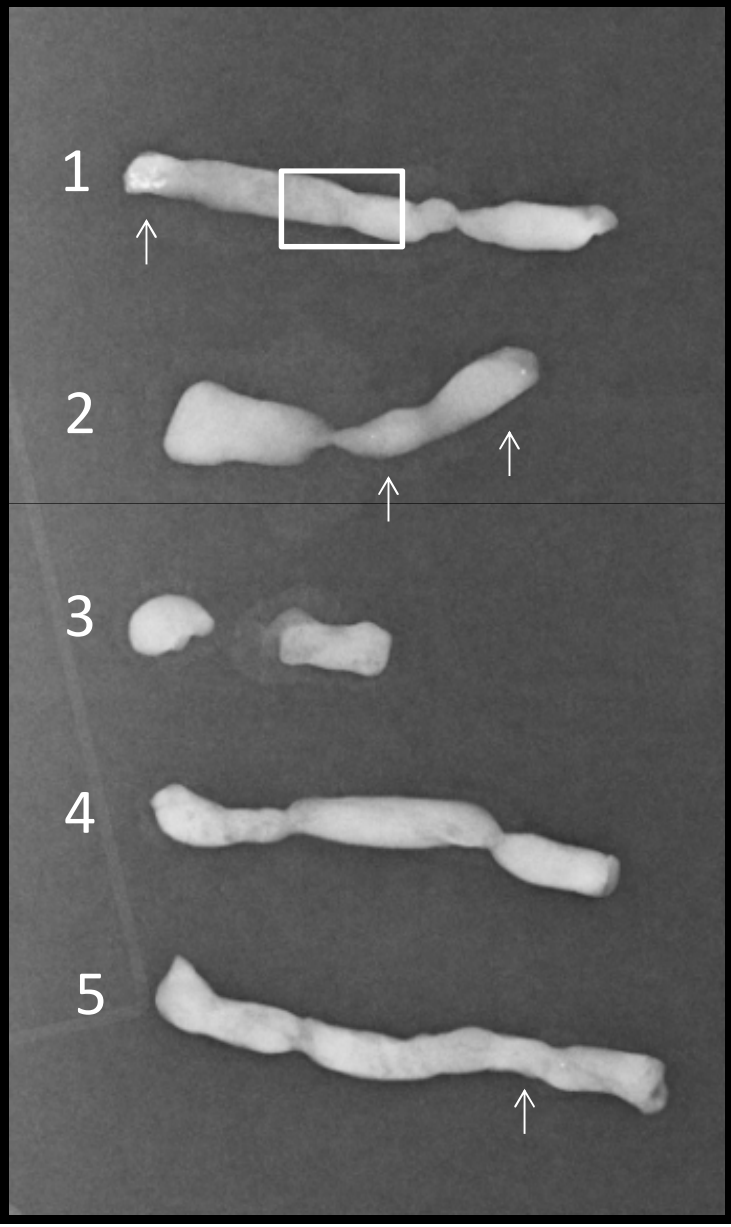
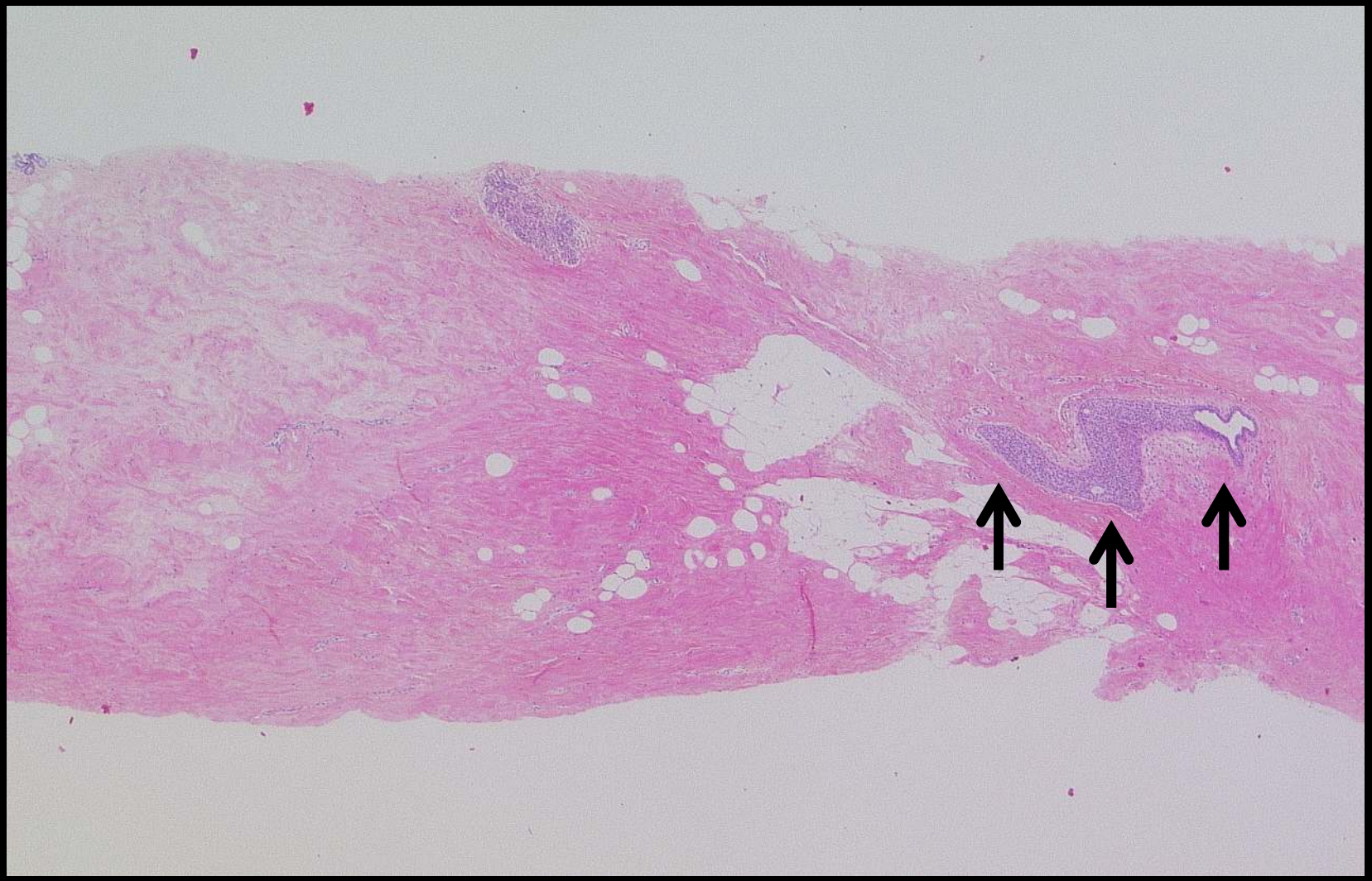
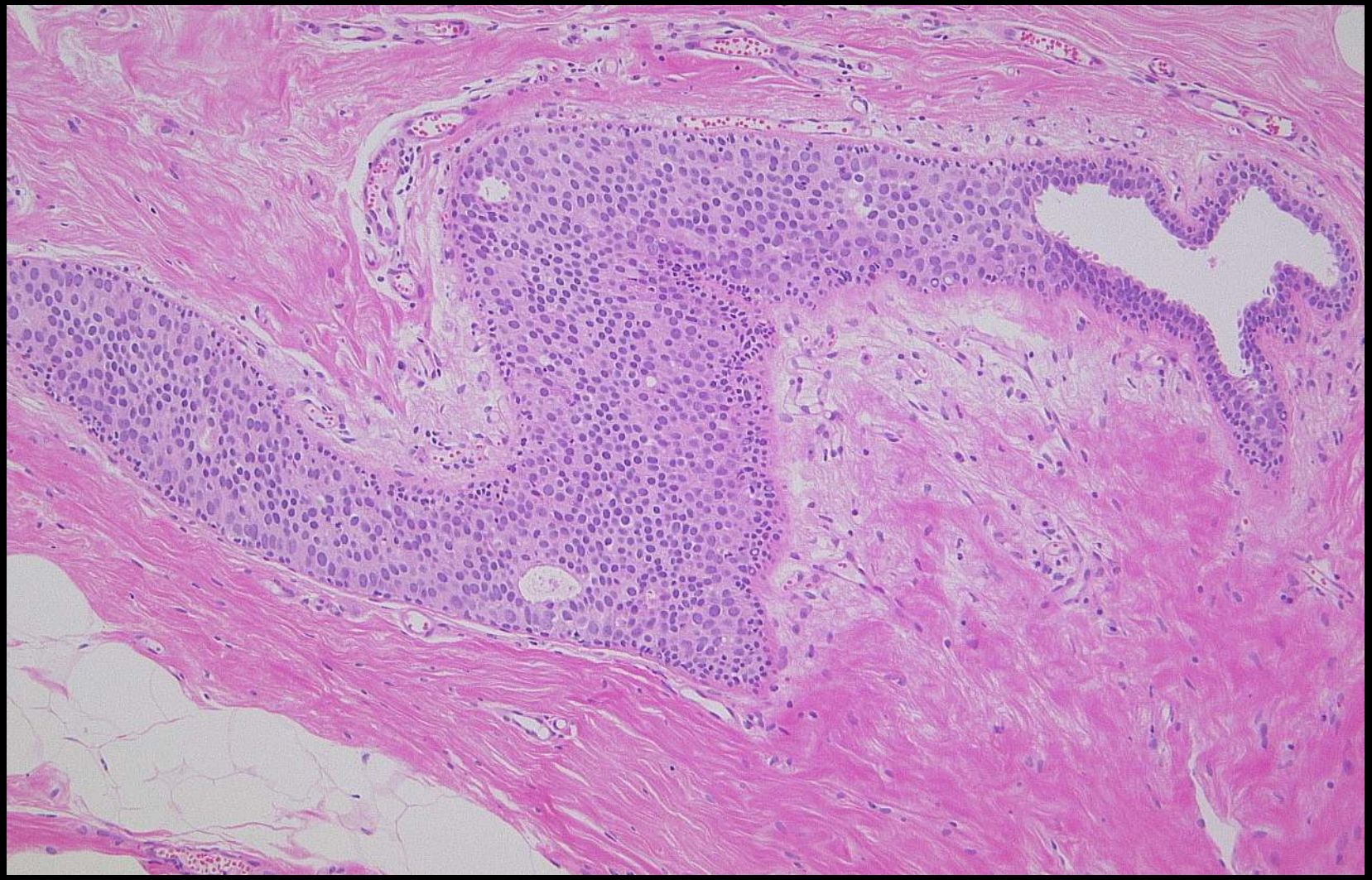




Original magnification: Objective lens X2

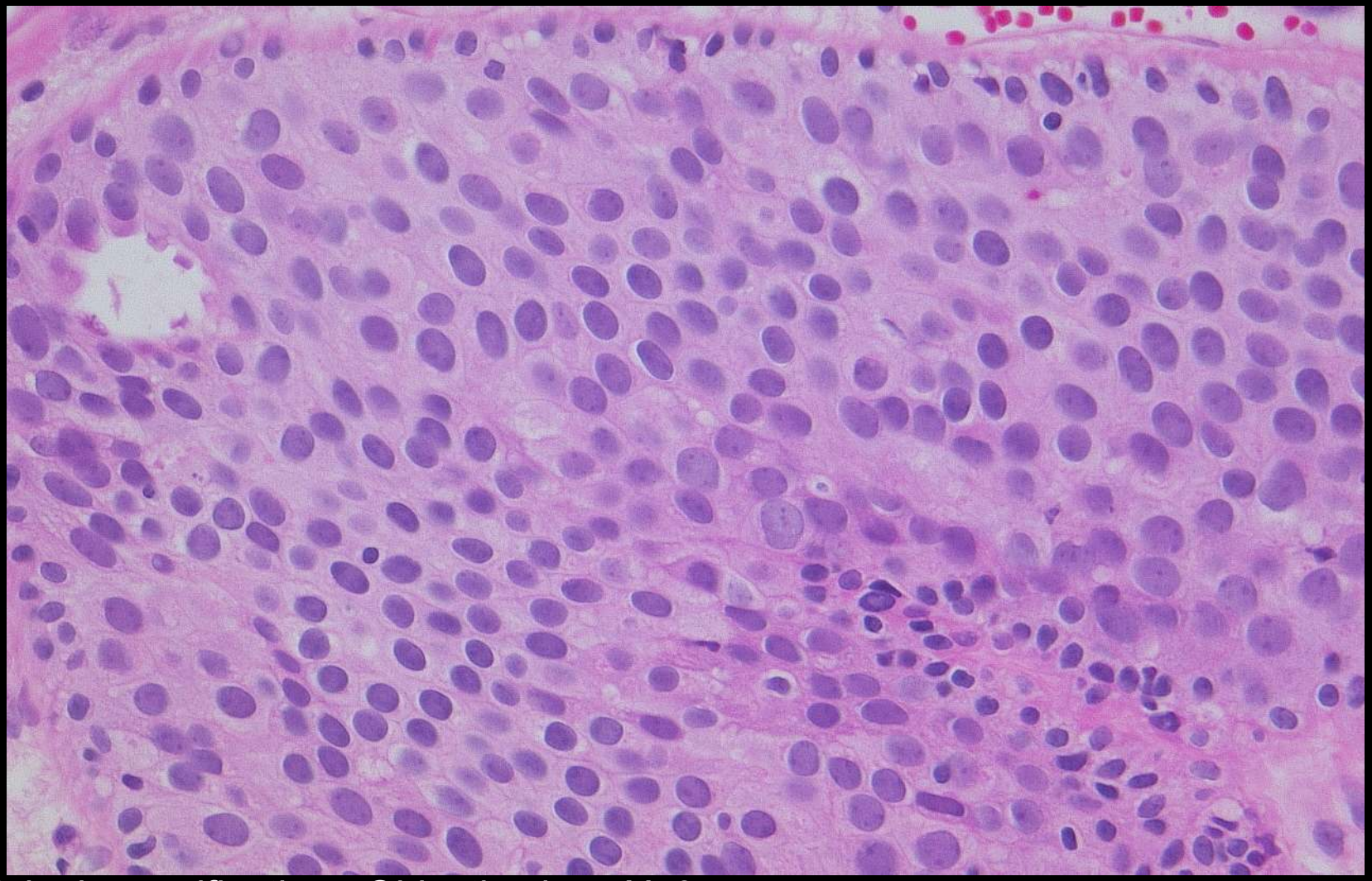
Atypical in situ lesion



Original magnification: Objective lens X10

A solid growth of monotonous atypical cells fills the duct lumen.

A few micro-lumens are evident.



Original magnification: Objective lens X40

These cells are cuboidal and have relatively abundant cytoplasm and oval nucleus with mild atypia. The myoepithelium is evident. This lesion was comparable to atypical ductal hyperplasia (ADH) according to the WHO histological classification.

Stereo-guided vacuum assisted breast biopsy
（Mammotome™ biopsy）

- 5 samples of 11 gauge needle biopsy
- Micro-calcifications were confirmed at 3 of 5 samples.
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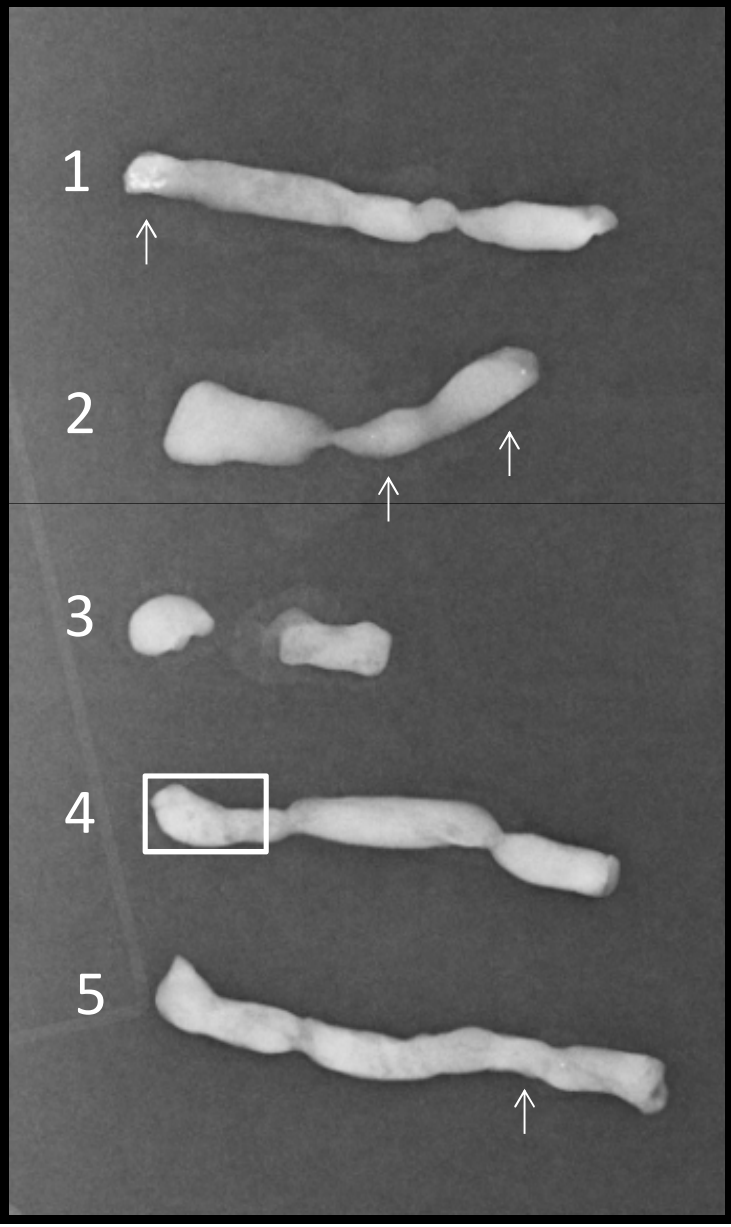
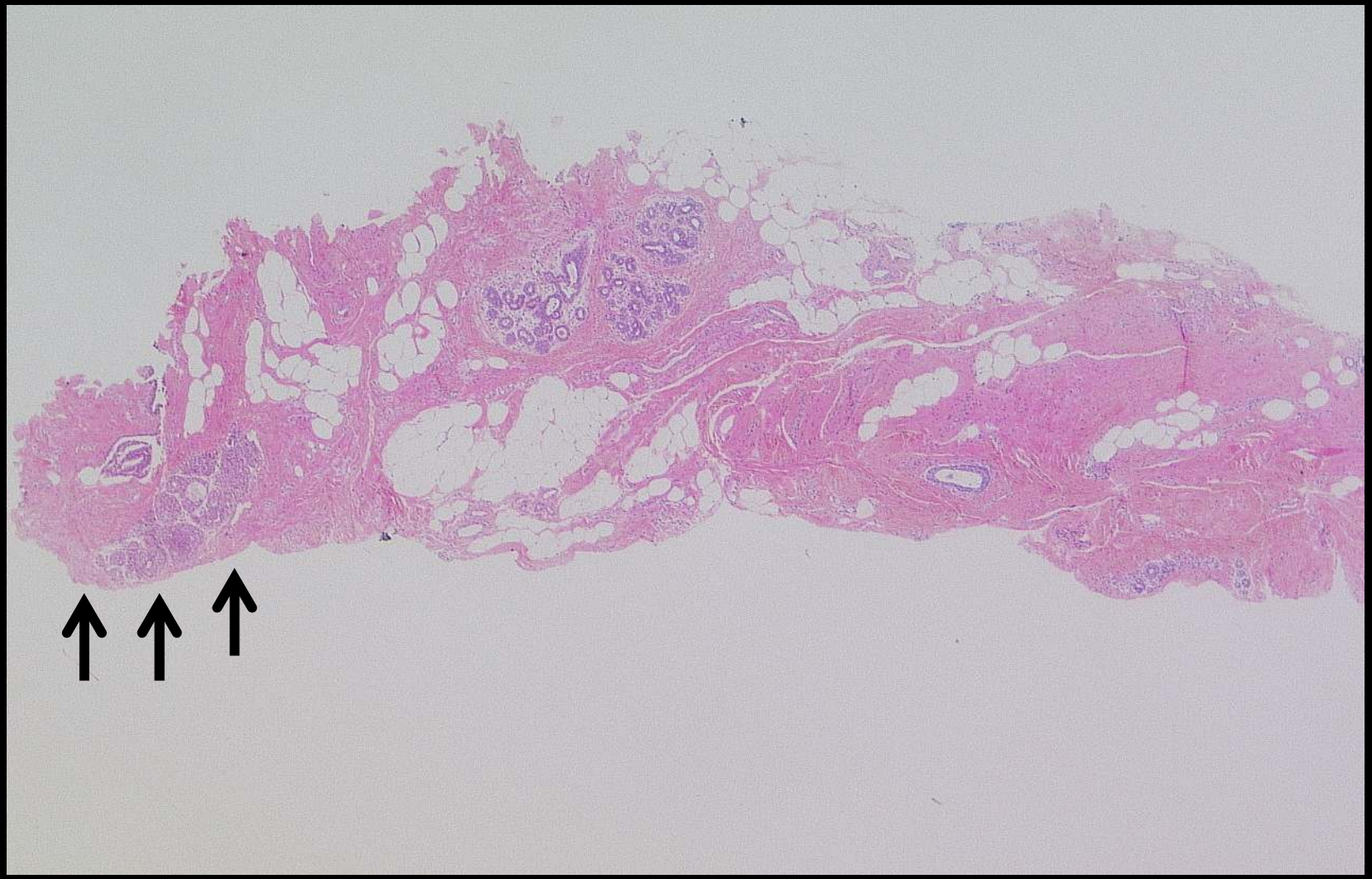
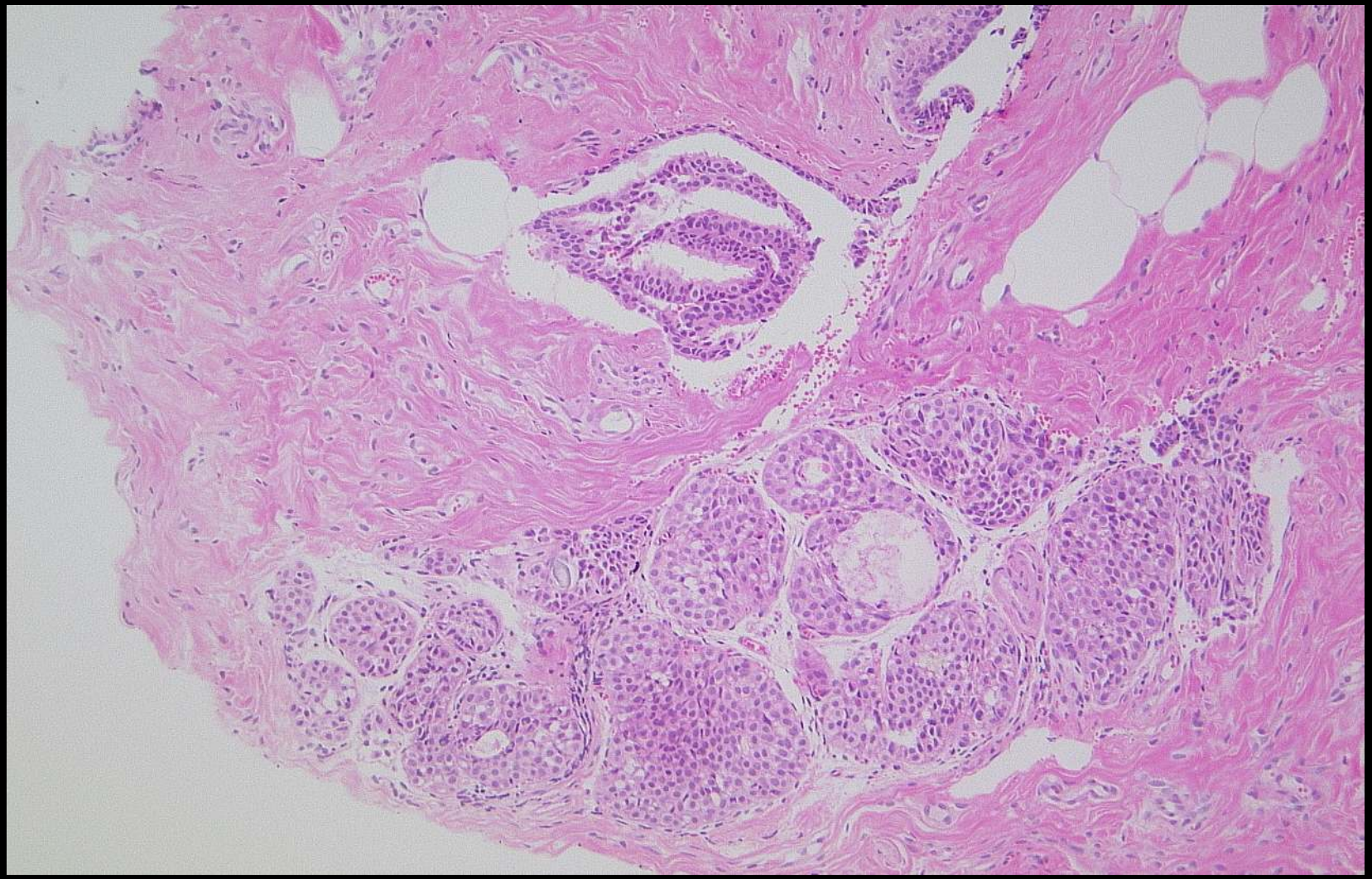




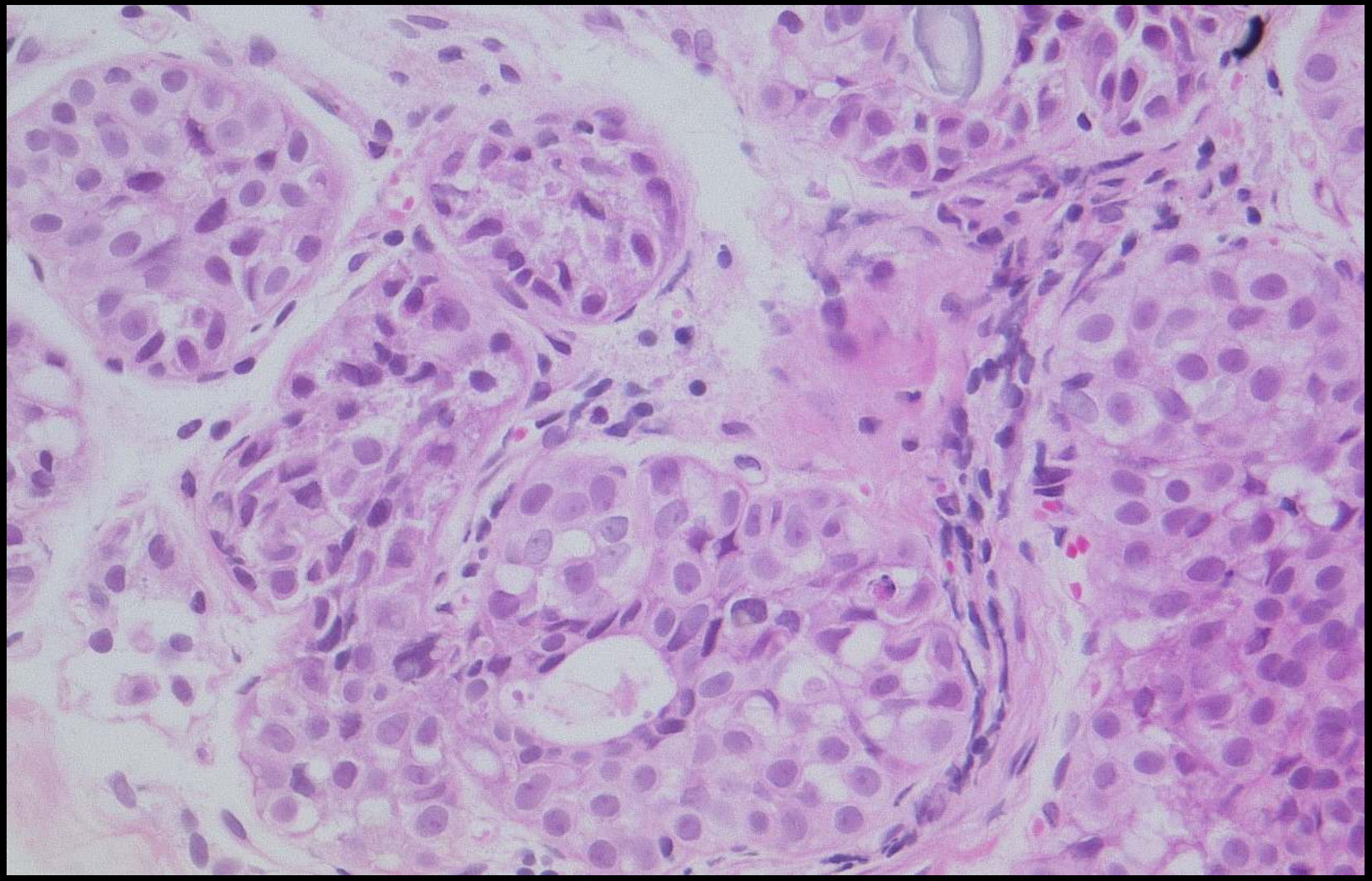
Original magnification: Objective lens X2

Atypical in situ lesion with micro-calcifications



Original magnification: Objective lens X10

A solid growth of atypical cells expands acini of a lobule.



Original magnification: Objective lens X40

These cells show mild atypia and loss of cohesion. This lesion was comparable to atypical lobular hyperplasia (ALH) according to the WHO histological classification.

Our diagnosis of the biopsy specimens

Atypical in situ lesion of the breast.

WHO histological classification

- Flat epithelial atypia (FEA)
- Atypical ductal hyperplasia (ADH)
- Atypical lobular hyperplasia (ALH)

Comments:

Benignity or malignancy cannot be determined.
Periodic follow up is needed.

1 year follow up

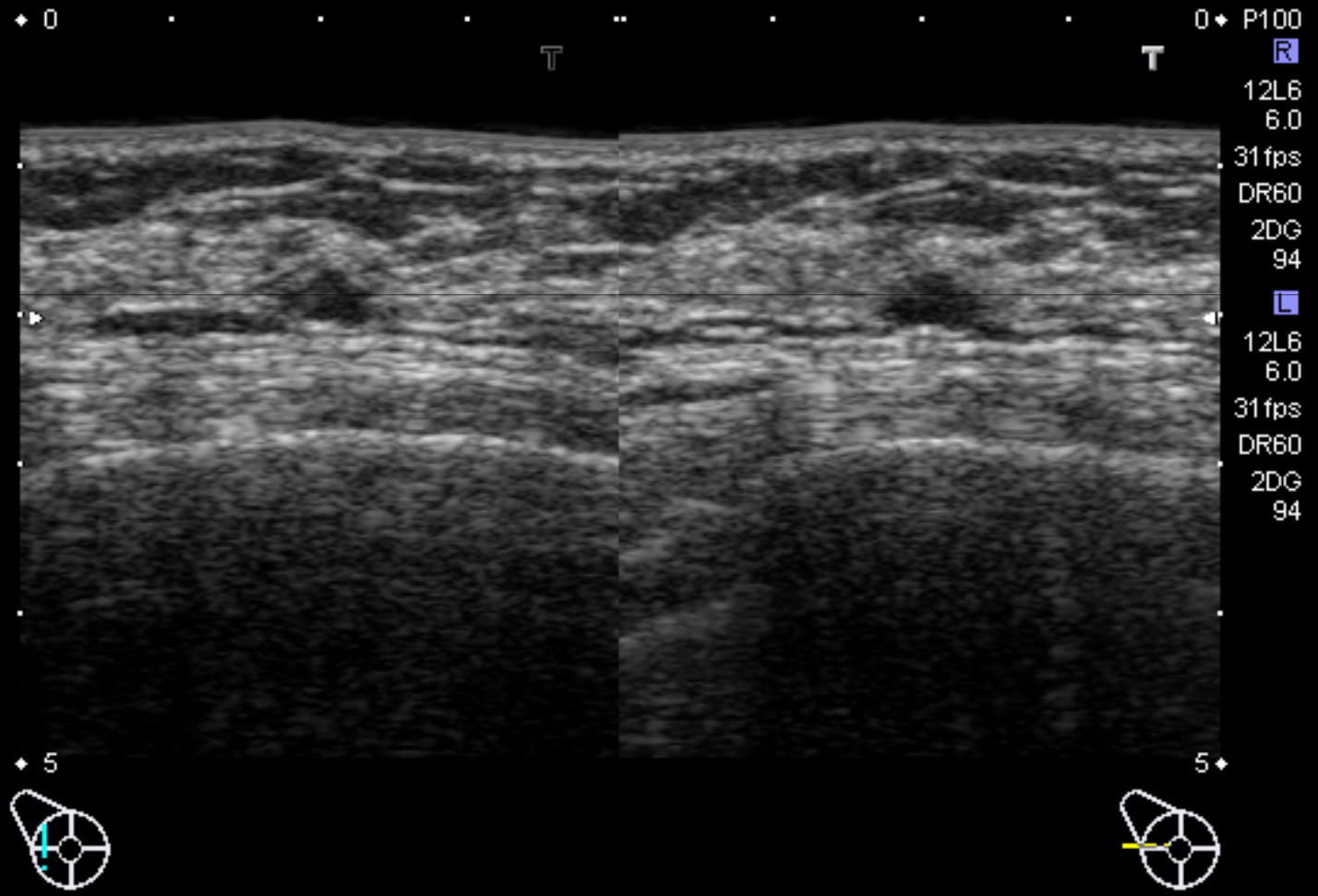
MMG: No change

US: Right outer upper area
Low echoic lesion, 5mm in diameter
Suspicious of concentrate cyst

2 years follow up

MMG: No change

US: Low echoic lesion, 7mm in diameter
(Is growth present?)



2 years follow up

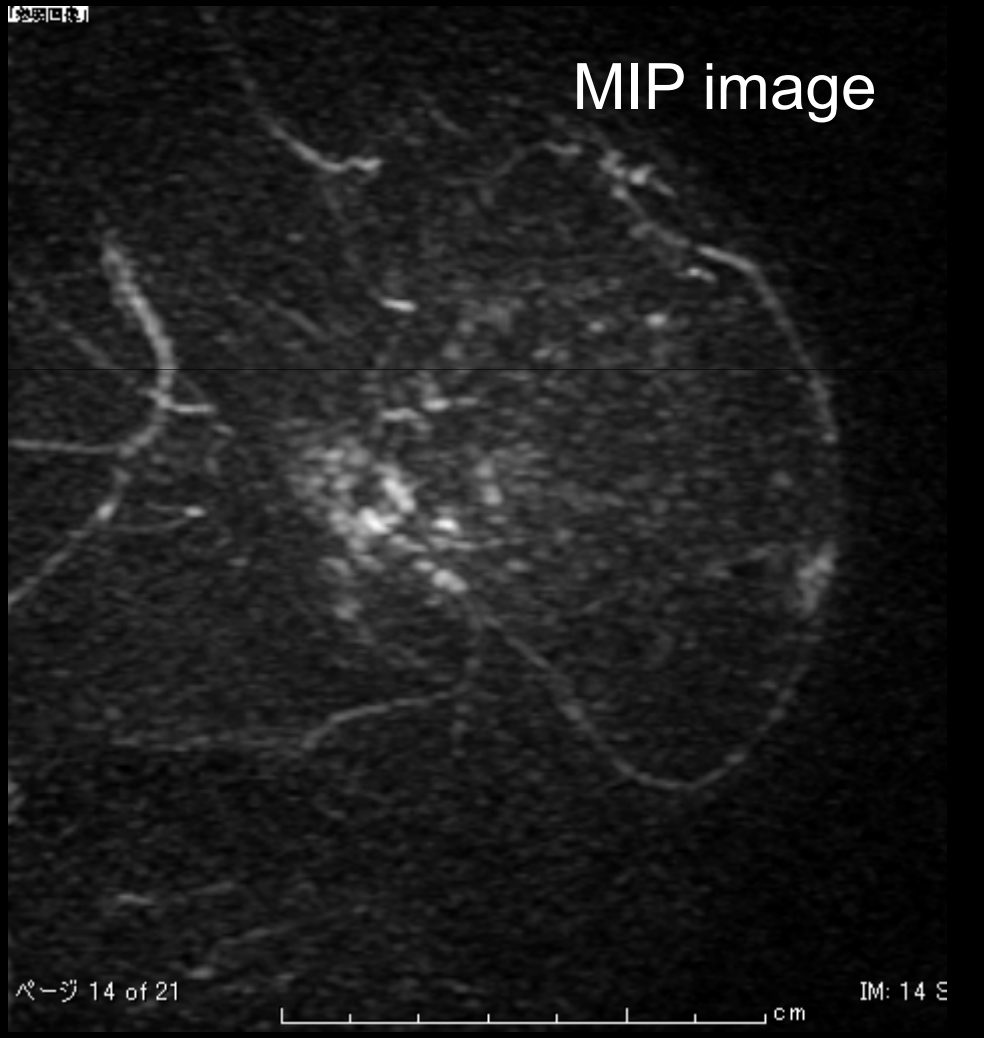
US-guided aspiration biopsy cytology was performed to the low echoic lesion in the upper outer area of the right breast.

Cytological diagnosis is suspicious of malignancy.

Preoperative MRI

Multiple small nodules are segmentally located near a micro-mark.

Suspicions of DCIS or micro-invasive breast cancer.



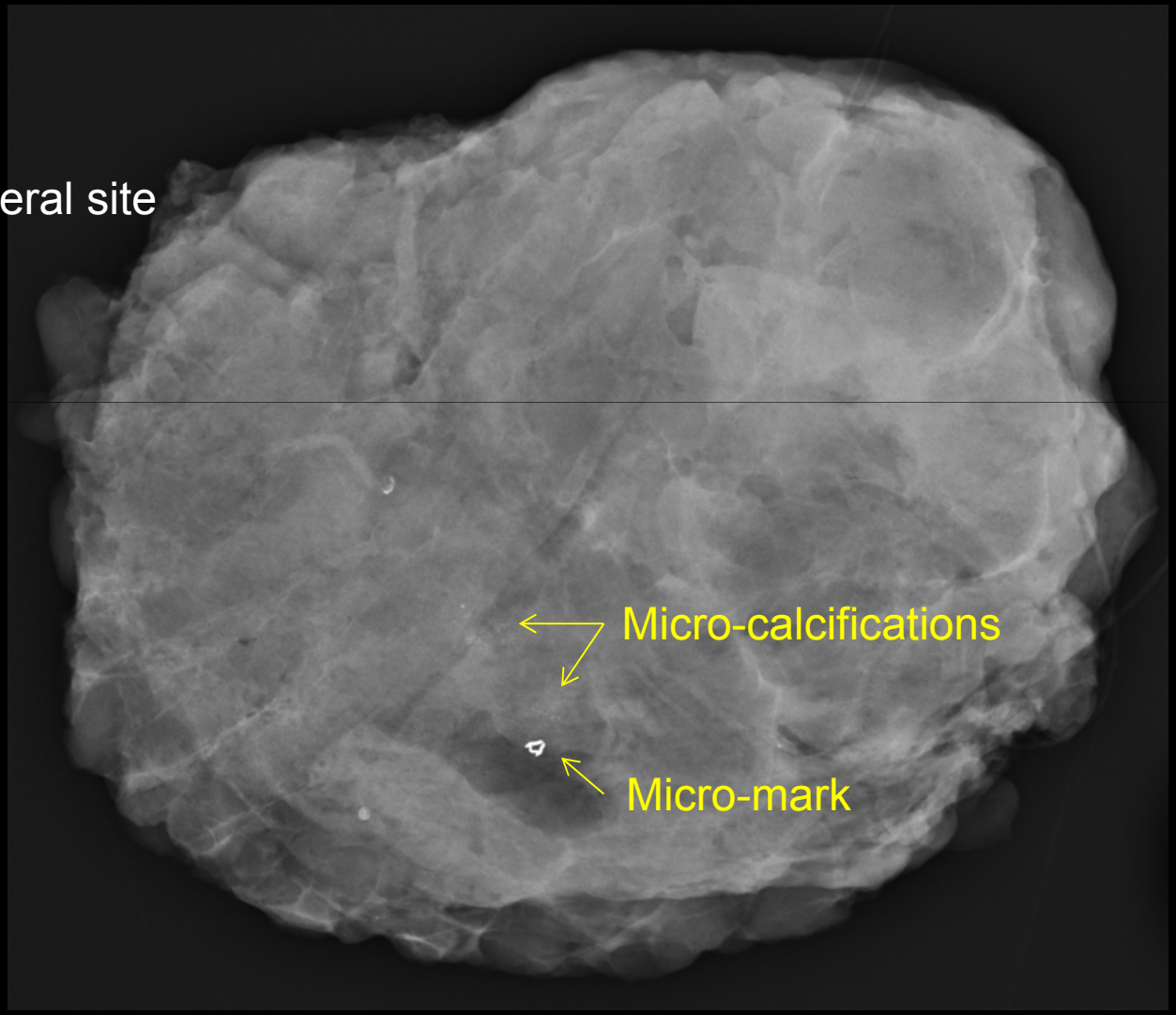
Operation

Right partial mastectomy with sentinel lymph node biopsy was performed.

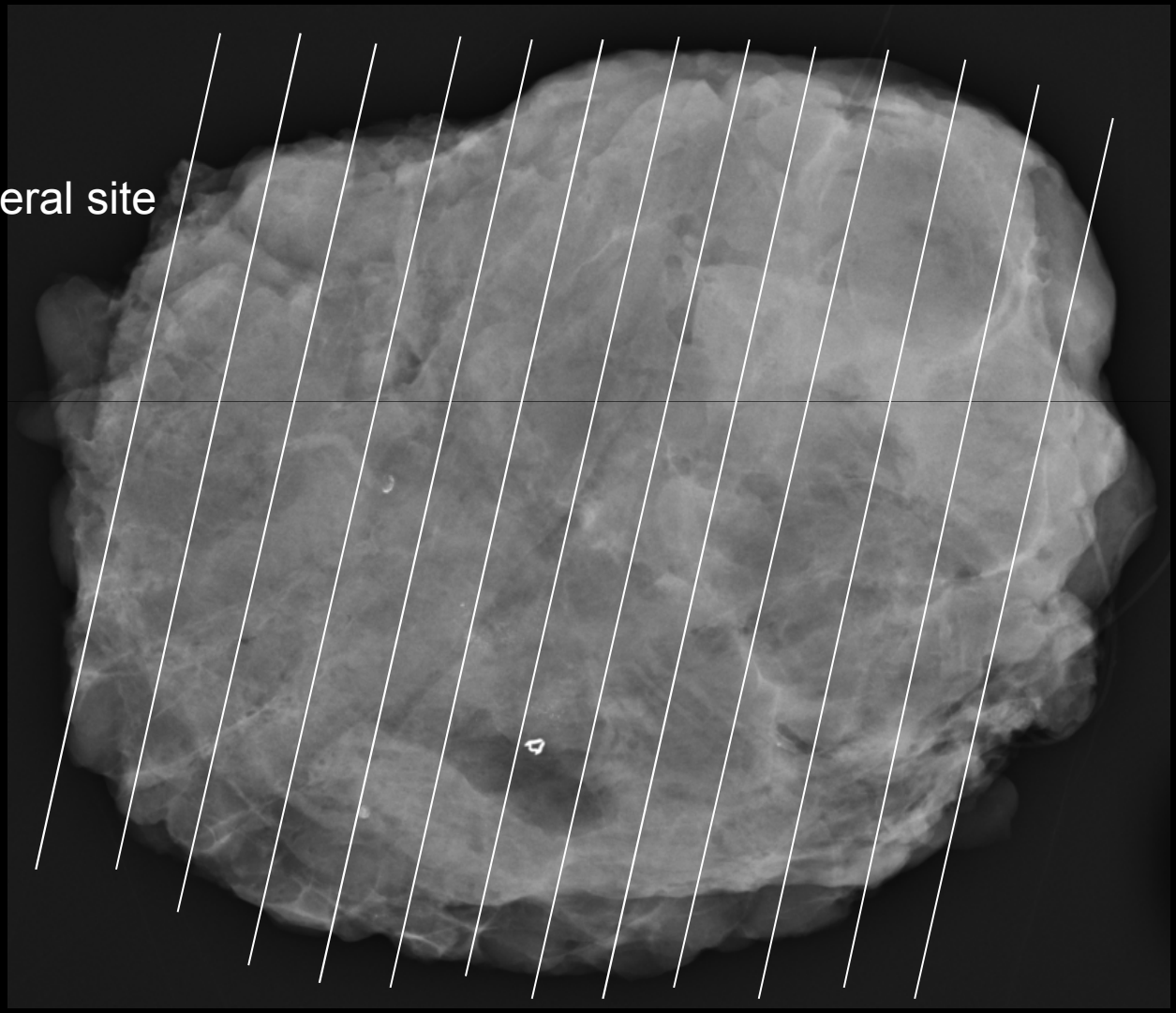
Sentinel lymph nodes showed negative for cancer by frozen sections during the surgery.

Axillary lymph nodes dissection was omitted.

Specimen mammography of the partial mastectomy material



Whole material is pathologically examined by 5 mm wide serial section

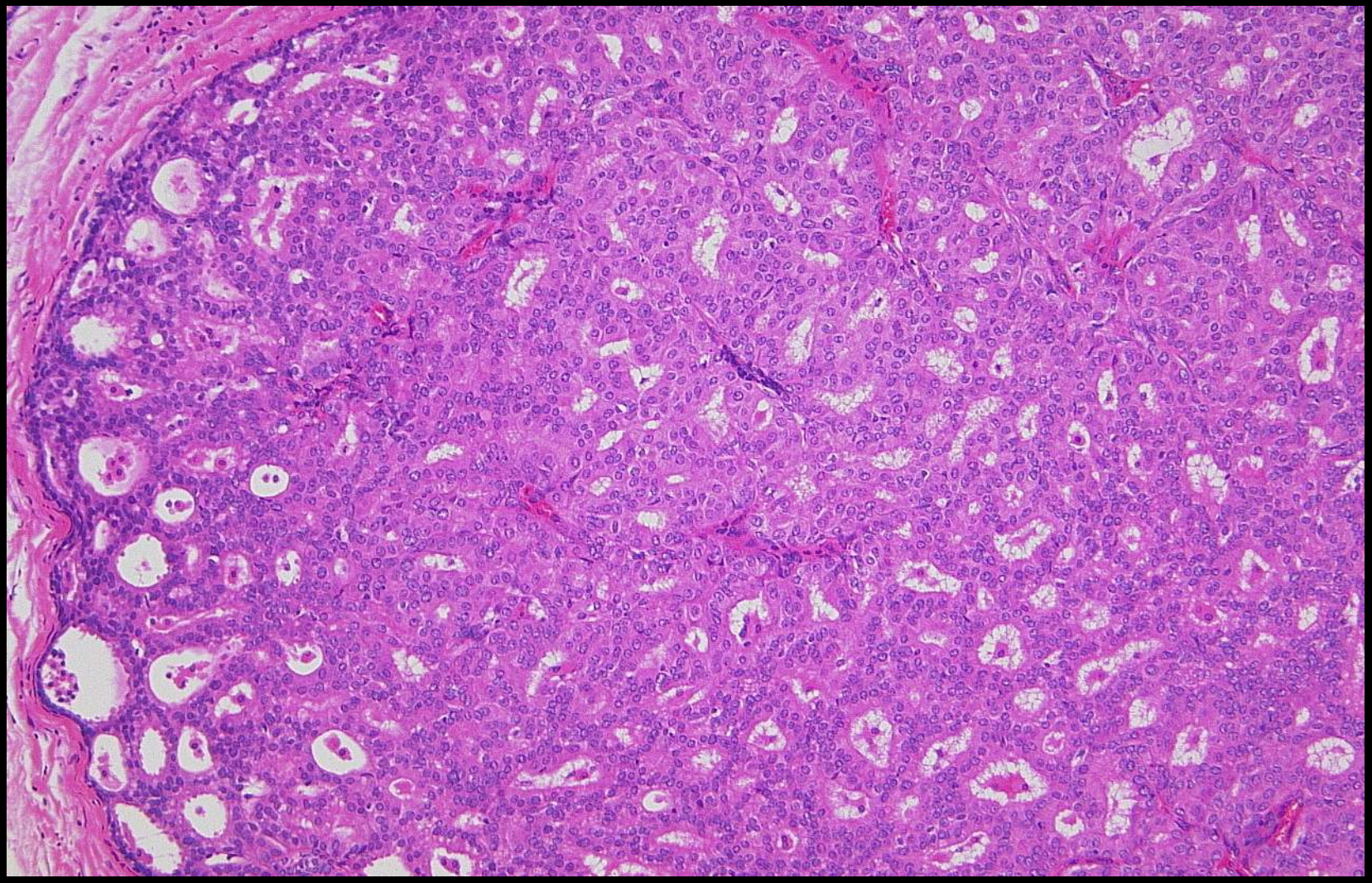


Pathological findings of surgical materials

Our diagnosis of the surgical materials

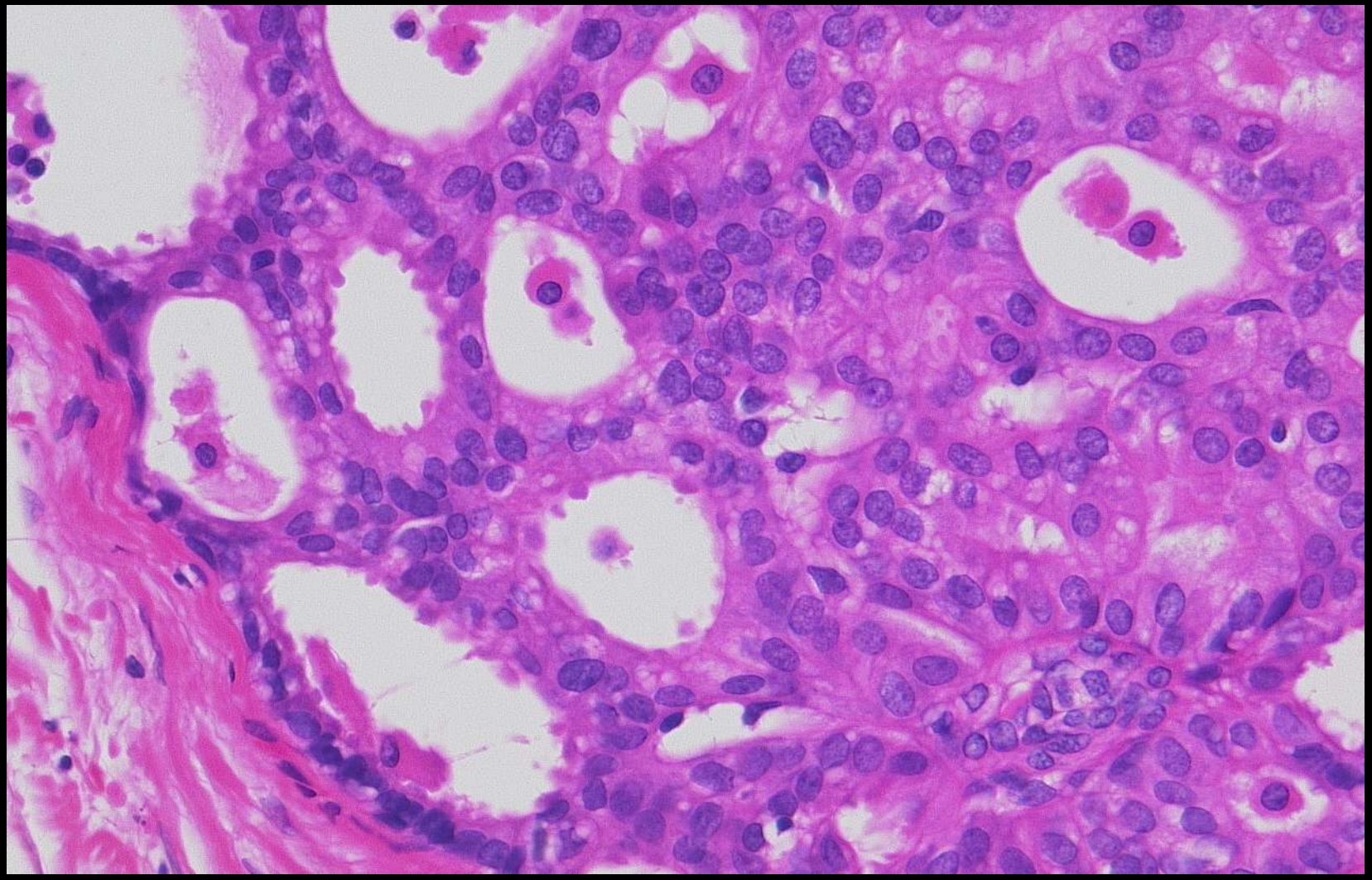
Noninvasive mixed ductal and lobular carcinoma of the breast.

Loupe image of the representative section



Original magnification: Objective lens X10

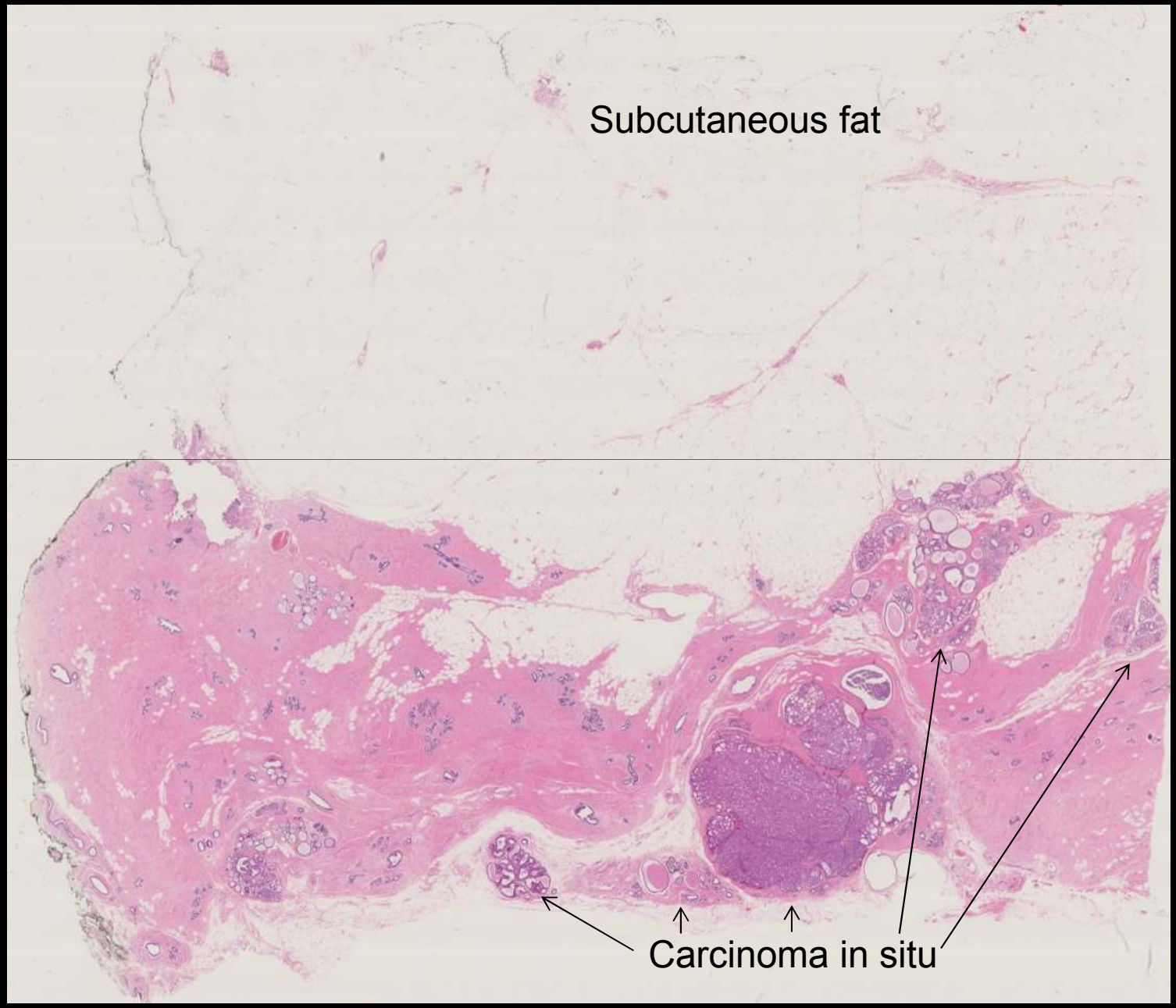
US-detected lesion shows histological findings of noninvasive ductal carcinoma, cribriform type.

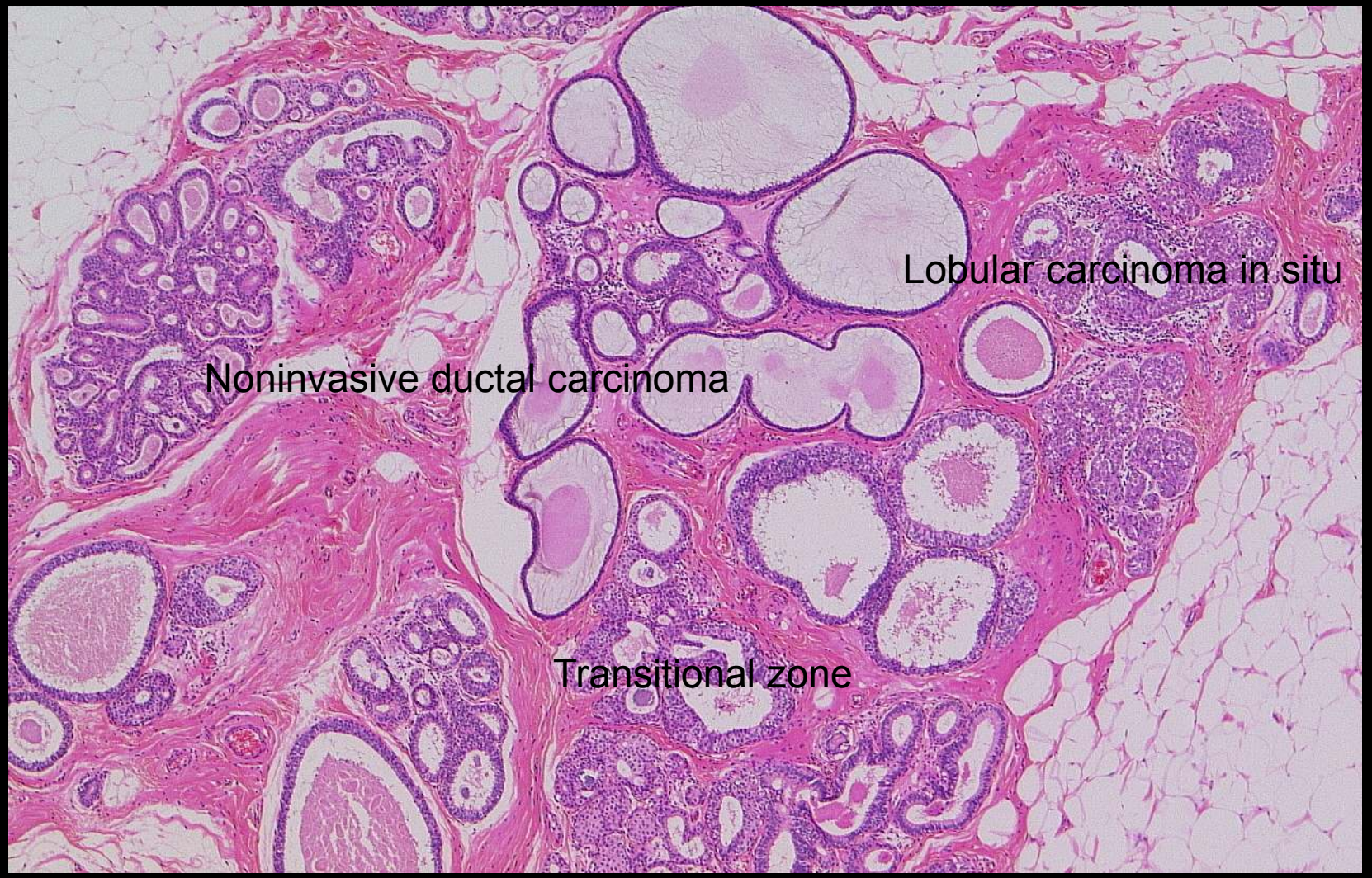


Original magnification: Objective lens X40

Cancer cells show the cribriform structure.

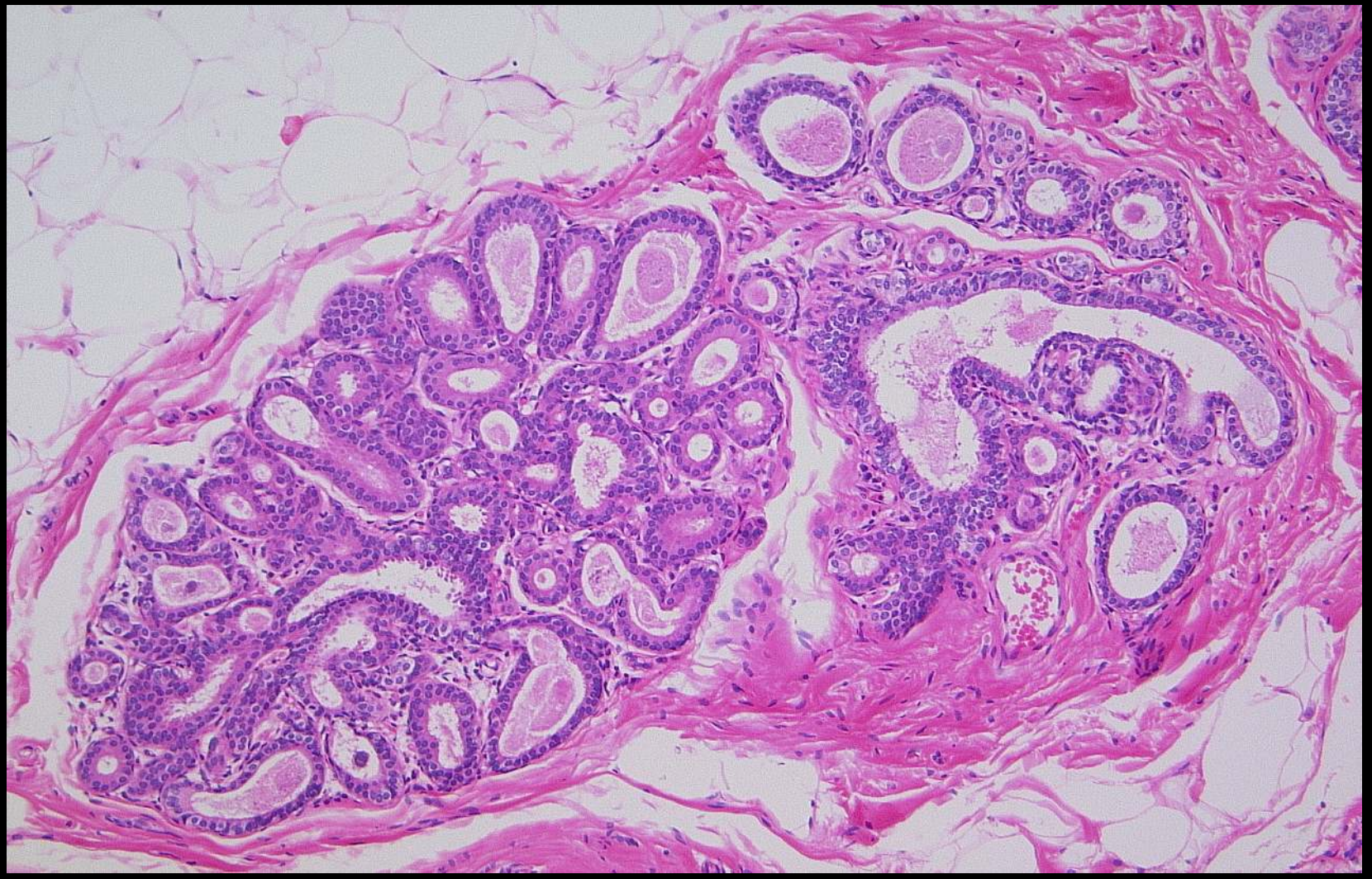
Loupe image of the representative section





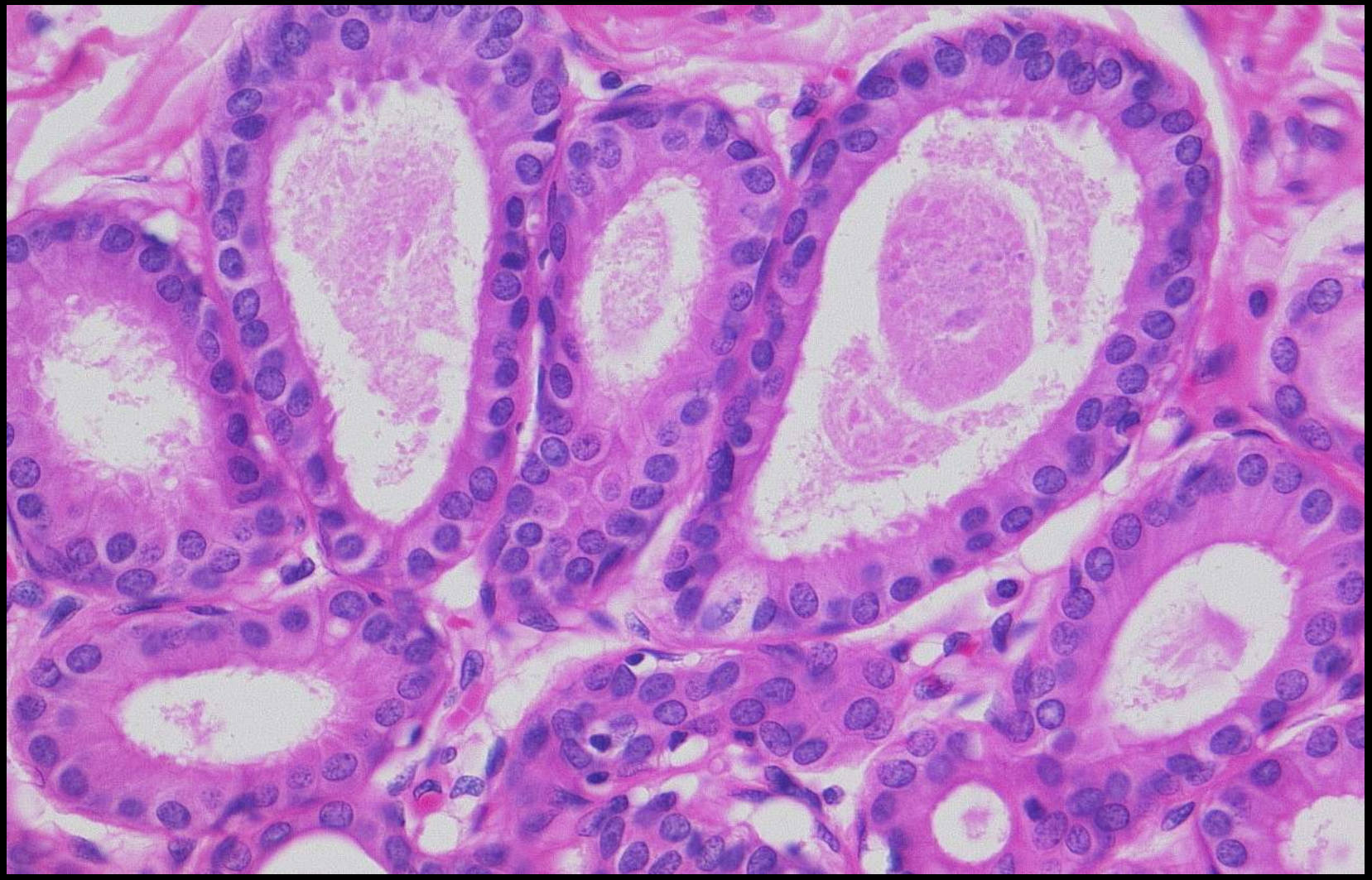
Original magnification: Objective lens x 4

Two distinct morphological patterns are seen in this area: noninvasive ductal carcinoma on the left and lobular carcinoma in situ on the right. Transitional zone between ductal and lobular carcinoma is seen on the center.



Original magnification: Objective lens X10

Noninvasive ductal carcinoma, flat type.

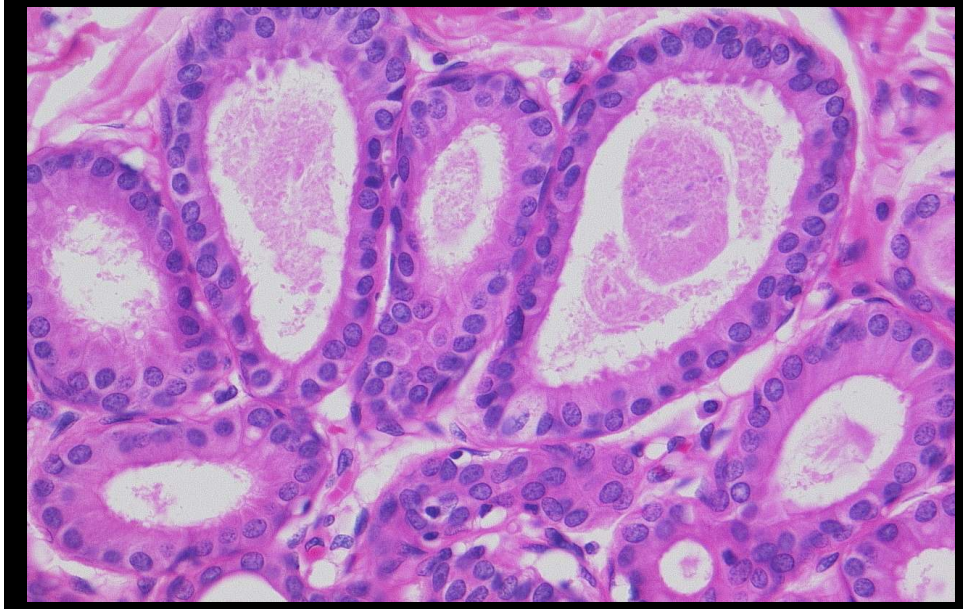


Original magnification: Objective lens X40

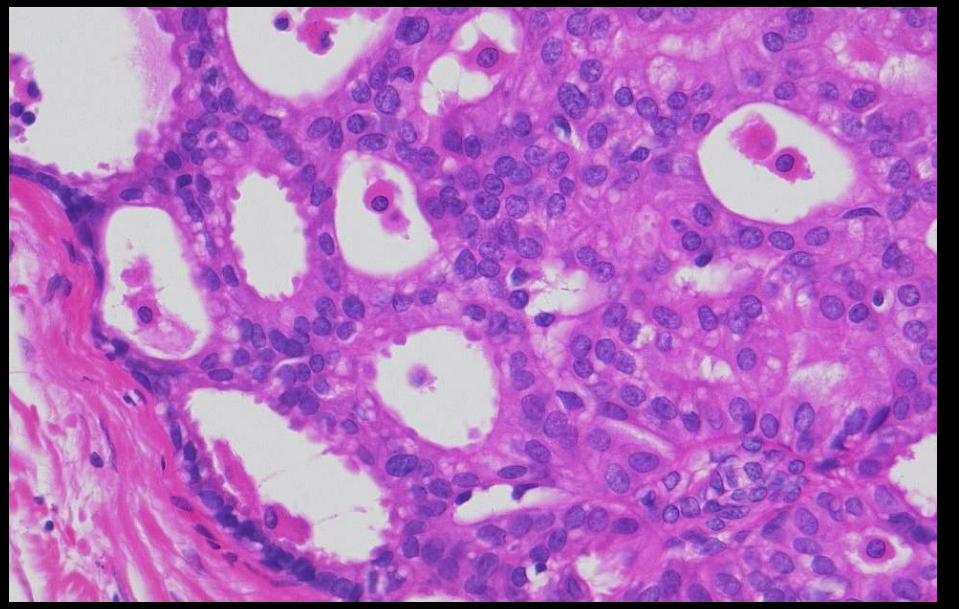
Noninvasive ductal carcinoma, flat type.

Noninvasive ductal carcinoma

Flat type



Cribriform type



Original magnification: Objective lens X40

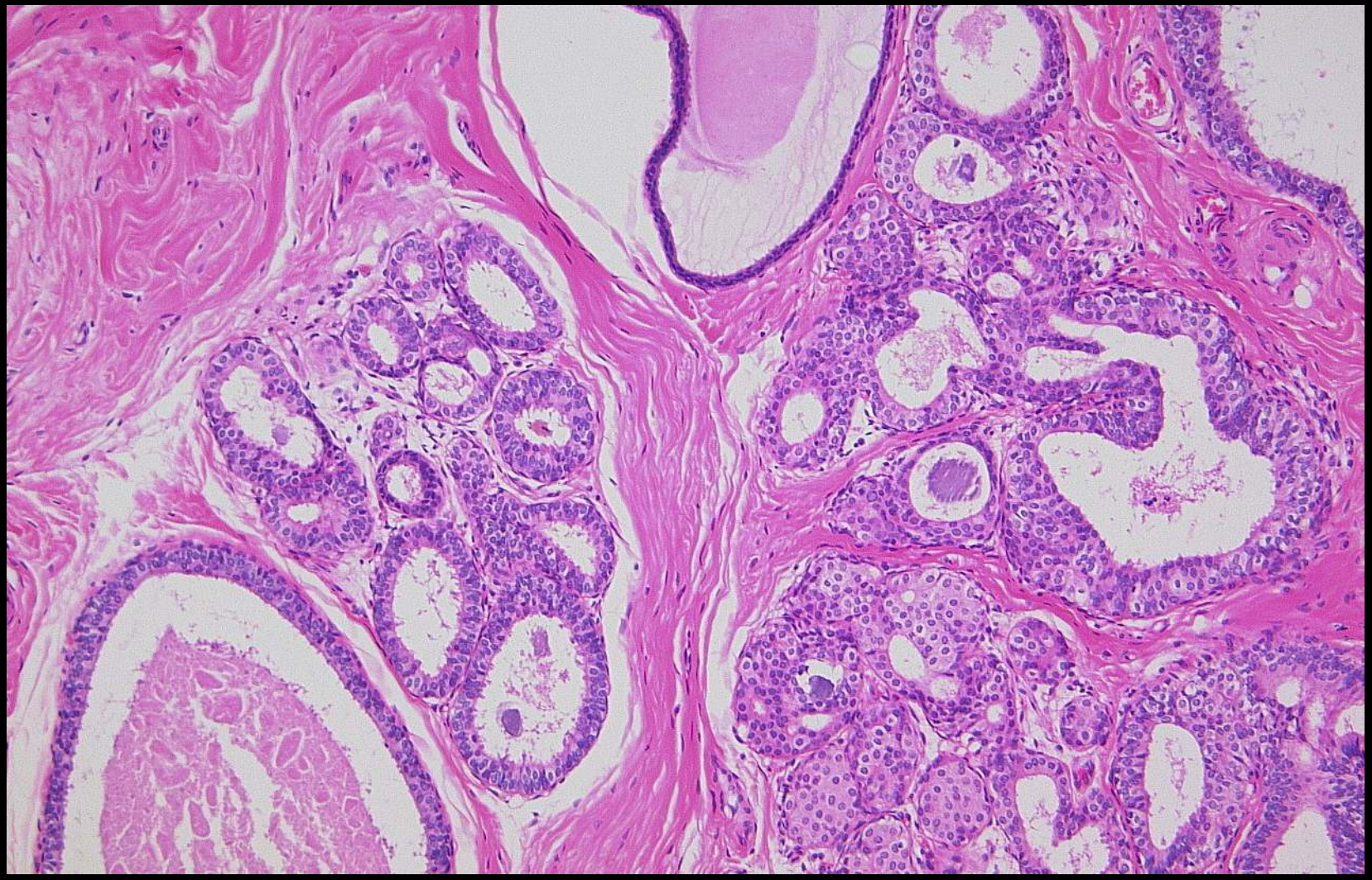
Cancer cells have relatively abundant cytoplasm, round to oval shaped nucleus and show tubular formations.

Original magnification: Objective lens X10

Lobular carcinoma in situ with a micro-calcification

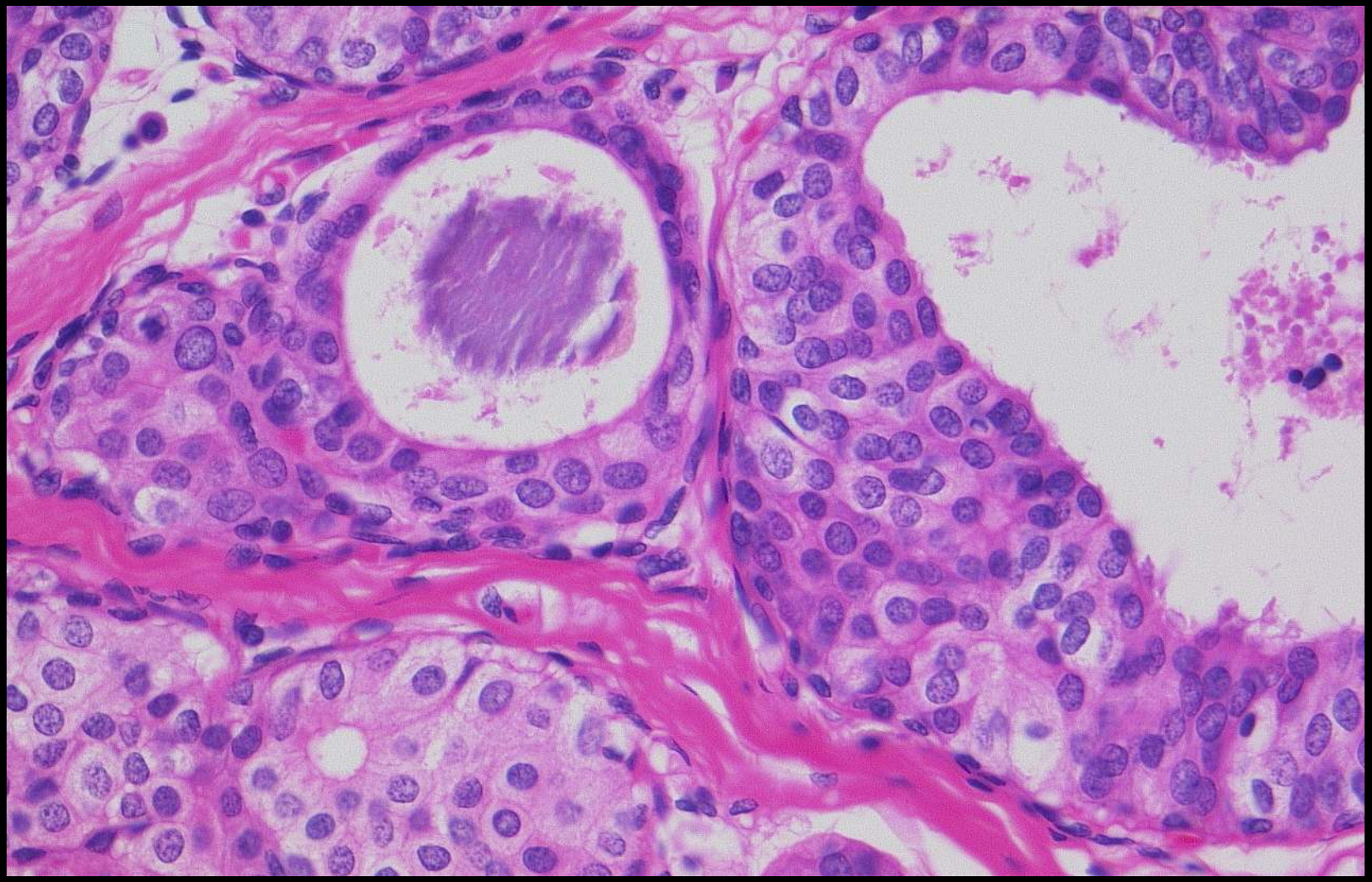
Original magnification: Objective lens X40

Loosely cohesive cancer cells proliferate beneath the native epithelial cell's lining (pagetoid growth pattern).



Original magnification: Objective lens X10

Transitional zone between ductal and lobular carcinoma with micro-calcifications



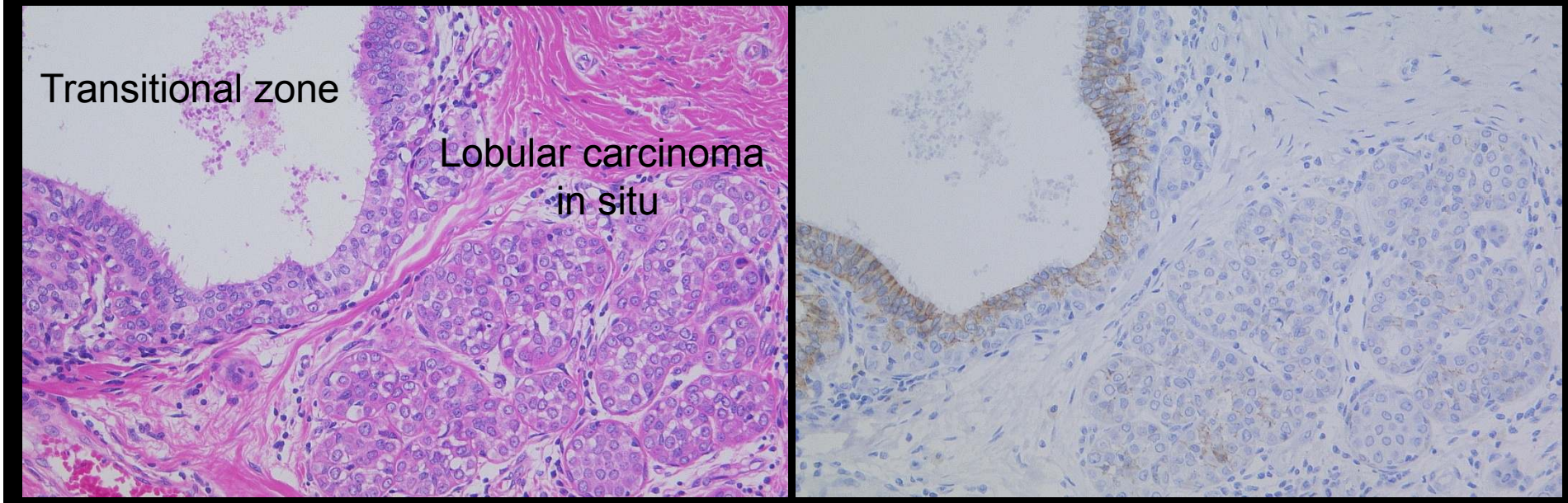
Original magnification: Objective lens X40

Histological structure of this area resembles those of lobular carcinoma in situ, but cancer cells appear more adherent than typical lobular carcinoma in situ.

Noninvasive mixed ductal and lobular carcinoma

HE

E-Cadherin



Original magnification: Objective lens X20

Two distinct morphological patterns are seen in this area:
lobular carcinoma in situ on the right and transitional zone on the left.
Lobular carcinoma cells show negative staining for E-Cadherinin.

Surgical margin: negative for cancer.

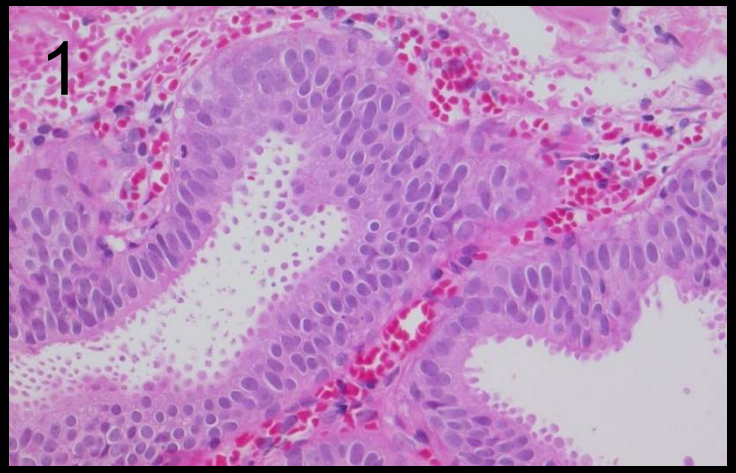
No lymph node metastasis

No adjuvant therapy

The patient is now alive without any recurrence 4 years after the surgery.

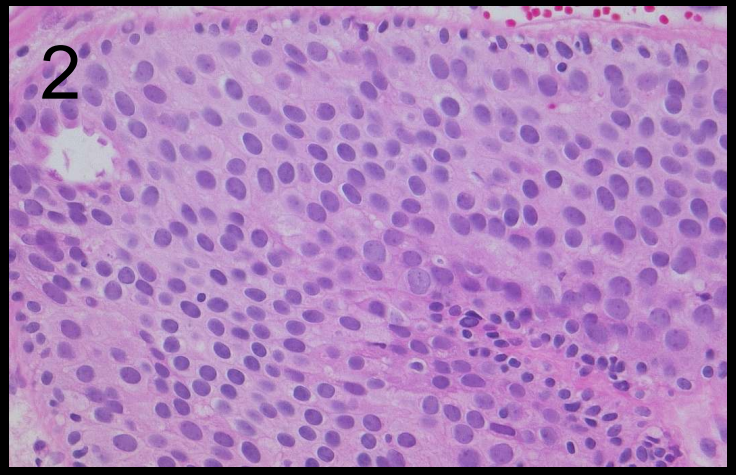
Review of pathological findings of biopsy specimens

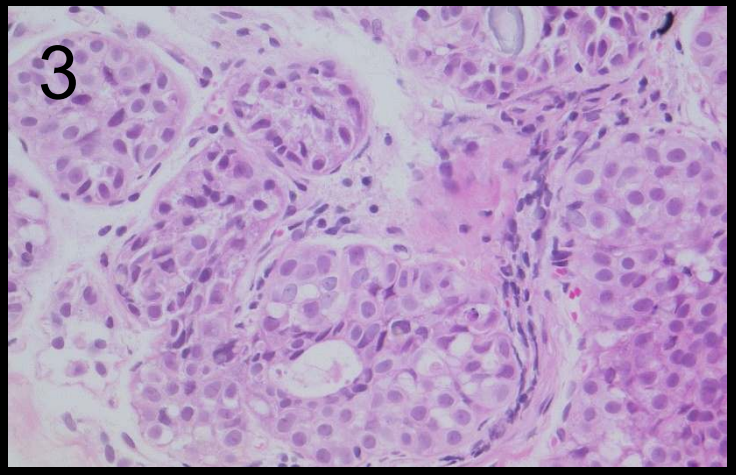
Our diagnosis of the biopsy specimens



Atypical in situ lesion of the breast

1. Flat epithelial atypia
2. Atypical ductal hyperplasia
3. Atypical lobular hyperplasia



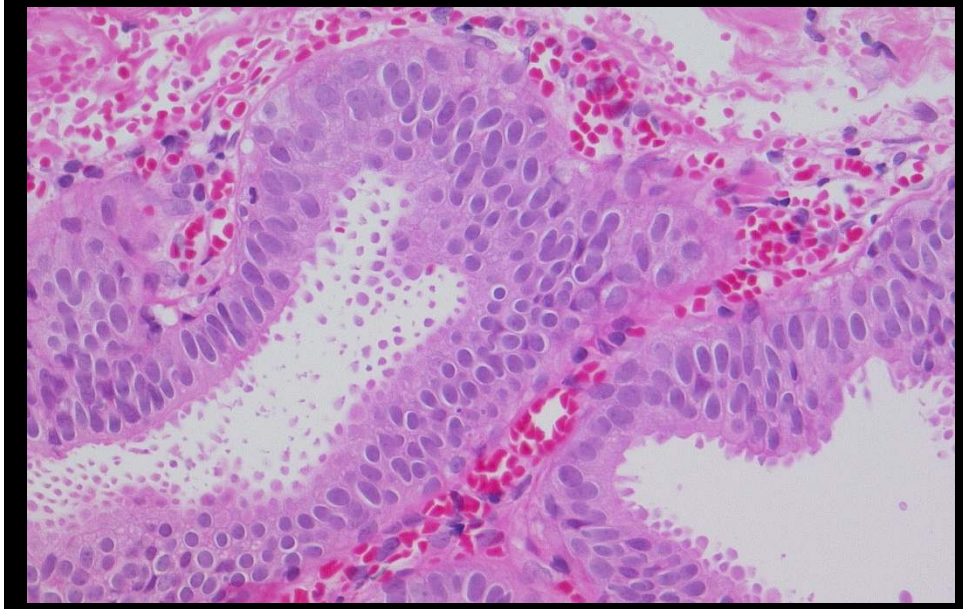


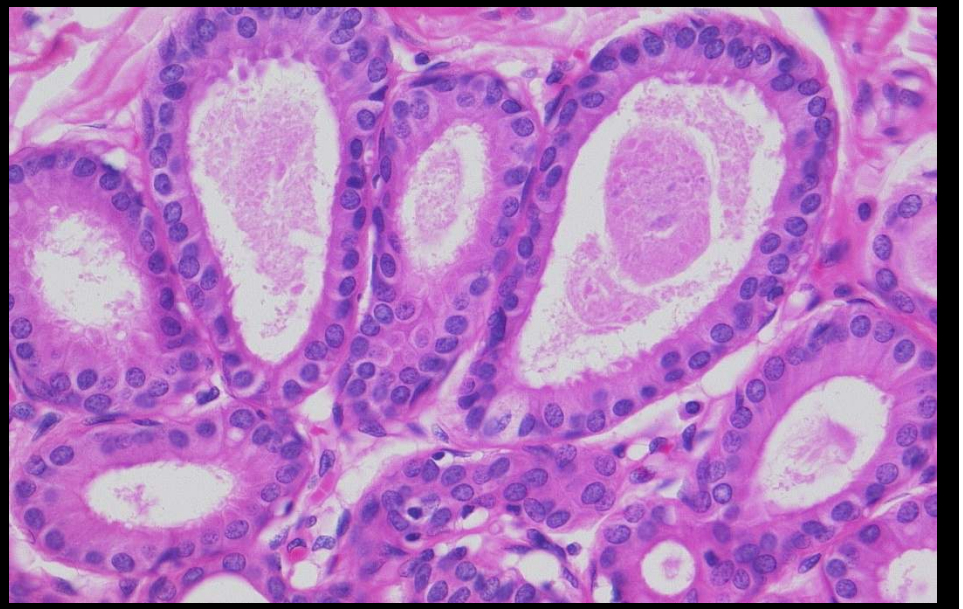
Biopsy specimen

Flat epithelial atypia

Surgical specimen

Noninvasive ductal carcinoma, flat type





Original magnification: Objective lens X40

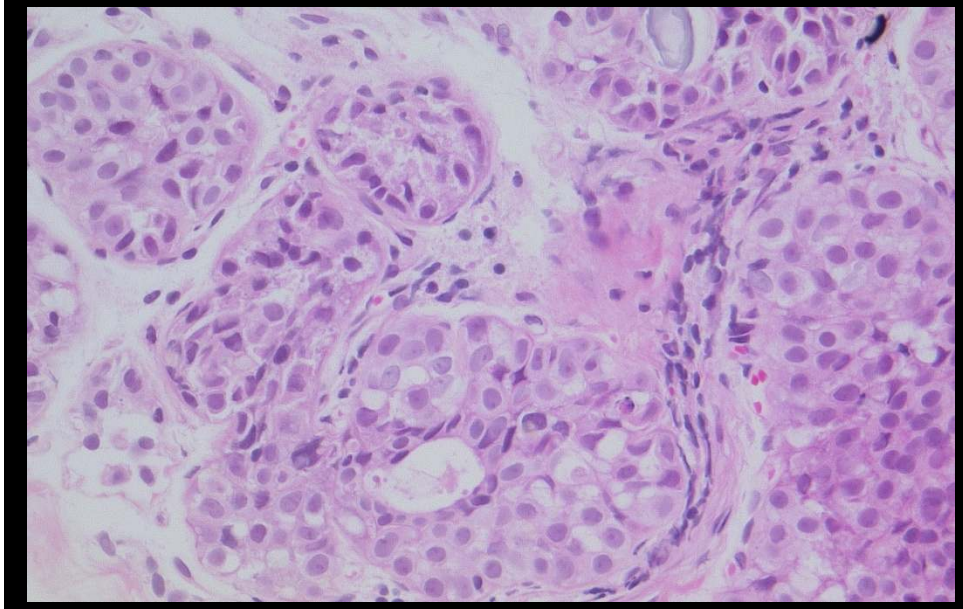
Pathological findings of FEA resemble those of noninvasive ductal carcinoma, flat type.

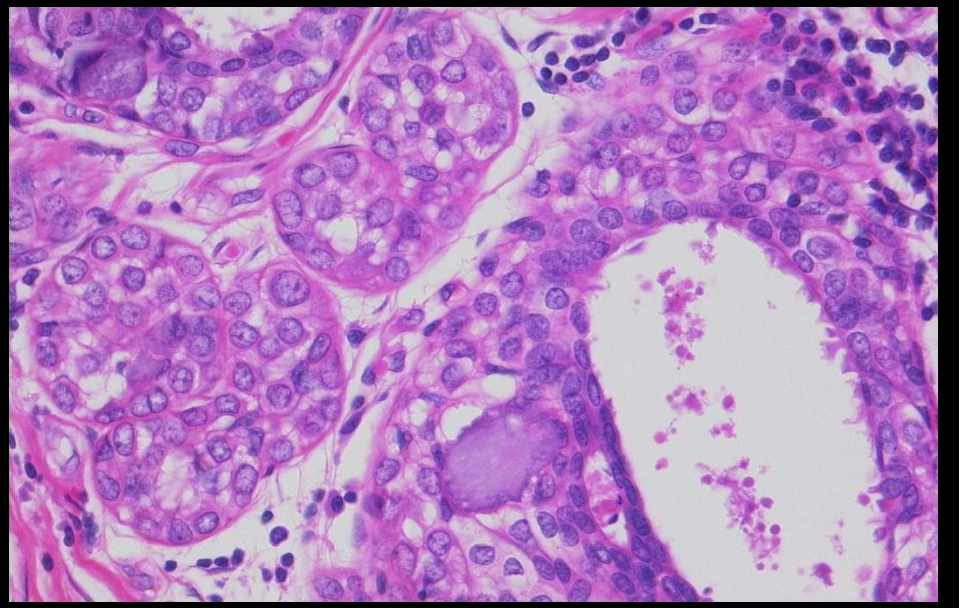
Biopsy specimen

Atypical lobular hyperplasia

Surgical specimen

Lobular carcinoma in situ



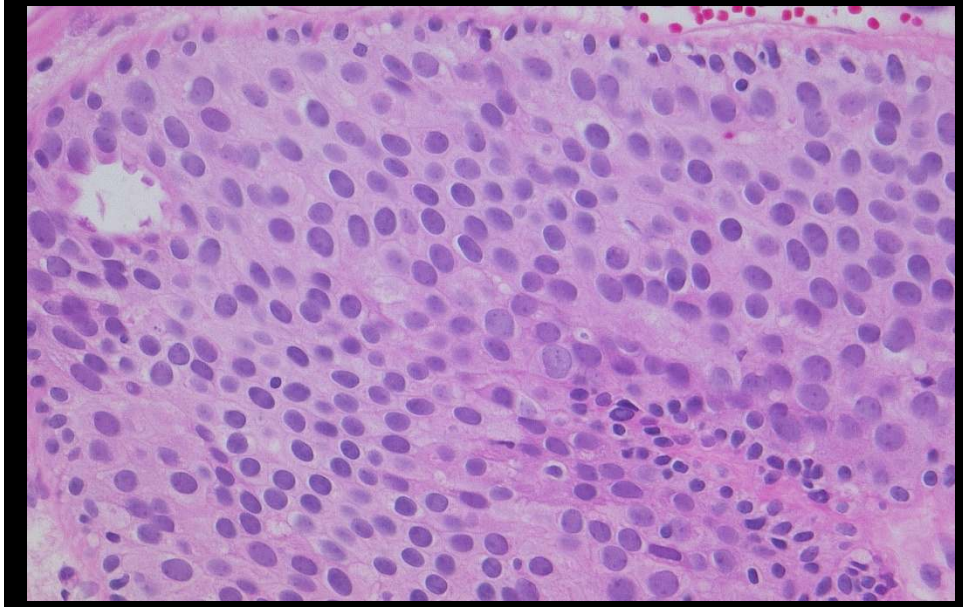


Original magnification: Objective lens X40

Pathological findings of ALH resemble those of lobular carcinoma in situ.

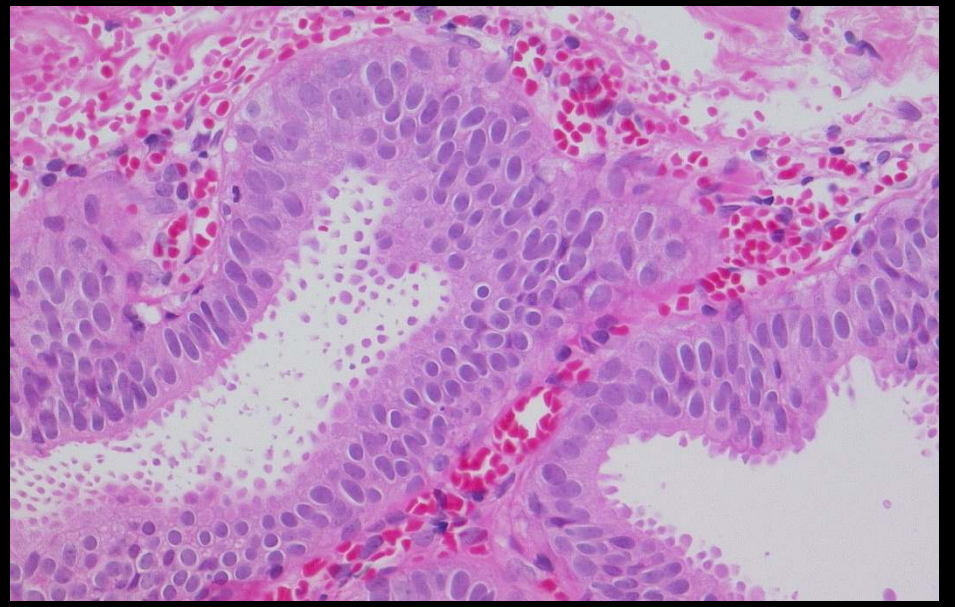
Biopsy specimen

Atypical ductal hyperplasia



Biopsy specimen

Flat epithelial atypia



Original magnification: Objective lens X40

Cytological findings of ADH resemble those of FEA.

Review of pathological findings of biopsy specimens

Lesions which were diagnosed as atypical in situ lesion in the biopsy specimens could be parts of noninvasive carcinoma.

Discussion points for the case

(A) Pathological diagnosis of this case

- Surgical specimen
- Biopsy specimen

(B) Management of this case after needle biopsy

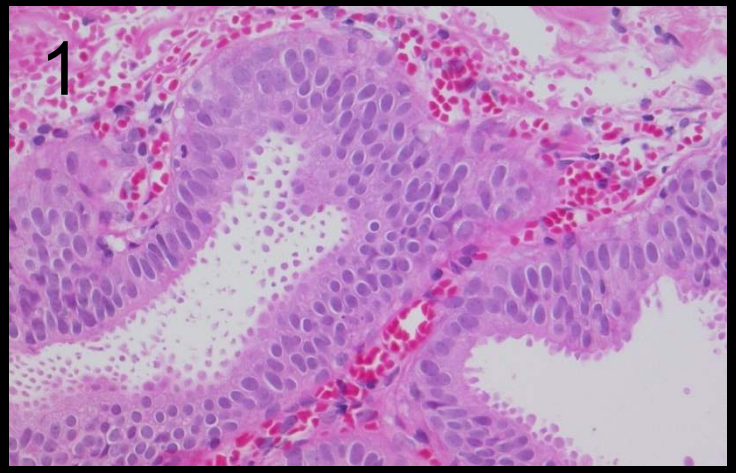
Our diagnosis of the surgical materials

Noninvasive mixed ductal and lobular carcinoma of the breast.

Discussion (A): Surgical specimen

- What would be your diagnosis of the surgical specimen?
- What would be your terminology of noninvasive carcinoma which have both ductal and lobular components?

Our diagnosis of the biopsy specimens



Atypical in situ lesion of the breast

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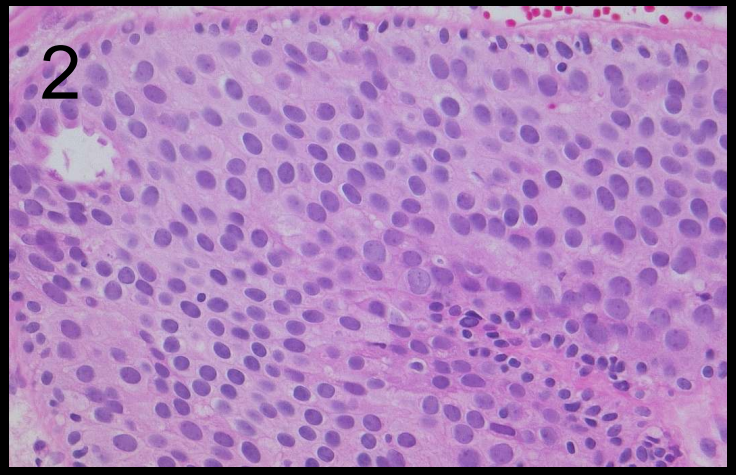

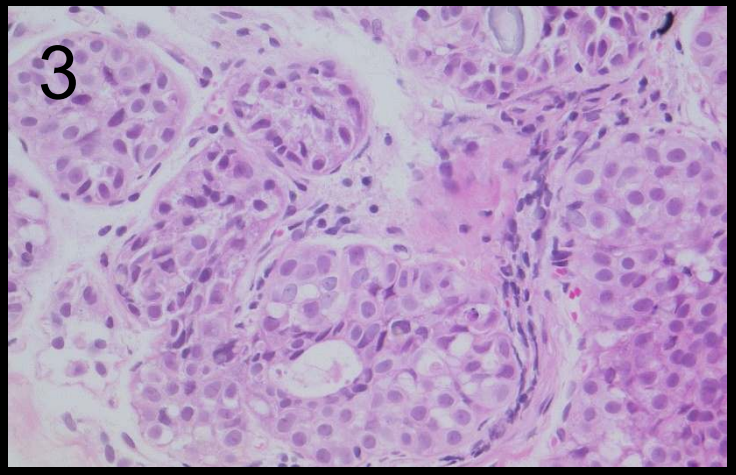

Discussion (A) : Biopsy specimen

- What would be your diagnosis of the biopsy specimen?
- After seeing the surgical specimen, did you change your diagnosis of the biopsy specimen?
- What would be your terminology of these lesions?

Mixed ductal and lobular carcinoma

Noninvasive carcinoma

- Noninvasive ductal carcinoma
- Lobular carcinoma in situ

Invasive carcinoma

- Invasive and/or noninvasive ductal carcinoma
- Invasive and/or noninvasive lobular carcinoma

Mixed ductal and lobular carcinoma

Mixed ductal and lobular carcinoma often contains noninvasive ductal carcinoma, flat type and lobular carcinoma in situ.

When only these components are sampled by a needle biopsy, pathological diagnosis of mixed ductal and lobular carcinoma is difficult.

Mixed ductal and lobular carcinoma should be considered, when both FEA and ALH are seen in a needle biopsy specimen.

Discussion (B):
Management of this case after needle biopsy

When atypical in situ lesion was found in needle biopsy specimen

- Excision?
- Re-needle biopsy?
- Follow up?
  - by MMG or US?
  - Interval?
  - Indication for re-biopsy?